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NEUROGLIAL CELL TUMORS

1. COMPUTED TOMOGRAPHIC APPEARANCES IN MICROGLIOMATOSIS.

Thomson JL, Brownell B
Dept. Neuroradiology, Frenchay Hosp., Bristol, England
Clin Radiol; 32(4):367-374 1981

The computed tomography (CT) appearances of 11 patients with microgliomatosis have been reviewed, and as a result it is possible to suggest that there may be typical features for the recognition of such tumors. In this series three fairly distinctive patterns were encountered. In view of their reputed response to radiotherapy, there is a strong case for making the diagnosis of such lesions, and CT has given the opportunity of alerting the surgeon and the pathologist to the likelihood of their presence at an early stage. (Author abstract) (10 Refs)

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2. MULTIMODALITY TREATMENT OF MALIGNANT GLIOMAS. COMPARISON OF SEVERAL ADJUVANT APPROACHES.

Jellinger K, Volc D, Grisold W, Podreka I, Bock F, Schuster H, Alth G, Kogelnik HD
Ludwig Boltzmann-Institut fur klinische Neurobiologie, Wolkersbergenstr. 1, A-1130 Wien, Austria
Zentralbl Neurochir; 42(2):99-122 1981

A controlled study compared the results of several chemotherapy protocols and/or radiotherapy in the treatment of 280 consecutive, age-matched patients with histologically confirmed Grade III and IV supratentorial gliomas (WHO classification) who had max feasible tumor resection, minimum postoperative survival of 4 wk, and a Karnofsky performance over 50. They were divided into seven groups: I. postoperative supportive care (110 cases); II. lomustine 100 mg/sq m every 6 wk (16 patients); III. Isreal protocol (procarbazine, 6-mercaptopurine, cyclophosphamide, amethopterine, 5-fluorouracil, and vinblastine) in 7-day cycles (15 cases); IV. megavoltage irradiation (40-60 Gy) without radiosensitizer (40 patients), V. radiotherapy (66 Gy) with radiosensitizer misonidazole (12 patients); VI. COMP protocol (CCNU, procarbazine, vincristine, amethopterine, and prednisone) in 15-day cycles (37 patients), and VII. simultaneous COMP chemotherapy and irradiation (40-66 Gy) (50 patients). Two hundred and sixty five patients were evaluated (valid study group). The recurrence-free intervals in all treatment groups (5.0 to 5.5 mo in groups II and III, and 6.3 to 11 mo in groups IV-VII) were significantly longer than in controls (3.4 mo). Second or more craniotomies for tumor recurrence were performed in 27% of the supportive care group and in 34 to 70% of the other groups, most frequently in groups VII, IV, VI and III (56-70%). Medium surviva was: controls 5.0 mo, CCNU 7.7 mo, Israel 8.6 mo, radiotherapy 11.6 mo, COMP chemotherapy 12.3 mo, radiation plus misonidazole 14.3 mo, COMP plus radiation (25 deceased patients) 13.1 mo, and 10 survivors 17.9 plus mo. The corresponding 1-yr survival rates were 3, 18, 26, 45, 67, and 73 (100)%. All groups showed considerable differences in the survival between grade IV and III gliomas: controls 3.9 vs 6.7 mo, radiation 7.3 vs 13.8 mo, COMP 9.5 vs 15.9 mo, and COMP plus radiation 11.5 vs 18.5 mo. The toxic side effects of multimodality treatment were moderate and essentially hematologic; 11.5% of the patients in groups VI and VII presented with space-occupying intracranial cysts simulating recurrences. These data indicate that combination of surgery, radiation and multiple-agent chemotherapy at present seems to be the most suitable treatment for anaplastic gliomas, but further trials for optimization of multimodality therapeutic approaches are warranted. (Author abstract) (68 Refs)

3. EVALUATION OF CCNU, VM-26 PLUS CCNU, AND PROCARBAZINE IN SUPRATENTORIAL BRAIN GLIOMAS. FINAL EVALUATION OF A RANDOMIZED STUDY.

EORTC Brain Tumor Group
(c/o Hildebrand) EORTC Brain Tumor Group, Cliniques Universitaires de Bruxelles Hopital Erasme, Route de Lennik 808, 1070 Brussels, Belgium
J Neurosurg; 55(1):27-31 1981

This prospective and randomized trial reports the effects of three chemotherapeutic regimens on three different clinical parameters in adults with supratentorial malignant brain gliomas: 1) duration of the interval between surgery and relapse (the 'free interval'); 2) total survival time; and 3) rate and length of objective remissions. All patients were irradiated with 5,500 to 6,000 rads after neurosurgery aimed at an optimum removal. The administration of 4'-dimethyl-epipodophyllotoxin-D-thenylidene-glucoside (VM-26), 60 mg/square meter (sq m) on Day 1, plus 1-(2-chloroethyl)-3-cyclohexyl-1-nitrosourea (CCNU), 130 mg/sq m on Day 2, repeated every 6 wk, had no significant effect on the length of the free interval between surgery and relapse. Thus, the median duration of this period was 39 wk in the group of 61 patients who received adjuvant chemotherapy and 30 wk in 55 controls without treatment. Neither was the total survival time prolonged by the administration of early chemotherapy. The best prognostic factor for the duration of the free interval and survival was age: patients under 50 yr old survived statistically significantly longer. The rate of the objective remission, defined as a clear-cut clinical improvement persisting 6 wk after complete discontinuation of steroids, was measured after tumor relapse. In patients who were not previously treated with chemotherapy, CCNU alone or VM-26 plus CCNU produced objective remissions in only 15% of treated patients. Out of 17 cases treated previously by VM-26 plus CCNU, none responded to procarbazine after relapse. (Author abstract) (8 Refs)

4. RADIO- AND CHEMOTHERAPY OF MALIGNANT GLIOMAS: EFFECTS ON THE TUMOR AND HEALTHY TISSUE (MEETING ABSTRACT).

Schiffer D, Giordana MT, Sciolla R, Soffietti R, Vasario E
Clinica Neurologica II, Universita di Torino, Turin, Italy
Tumori; 67(2,SupplA):78 1981

Forty-five brains of patients operated on for malignant glioma and treated with radio- and chemotherapy were examined. The effects of treatment were studied on full coronal sections of the brain. The necrotizing action on the tumor is expressed by an increase in cellular monstrosities, changes in the number of mitoses, the appearance of macrophages and vascular degeneration. Lesions of healthy nervous tissue must be differentiated from those produced directly or indirectly by the tumor, especially from those mediated by edema. Such lesions consist of peritumoral macrophagic and necrotic areas, vascular degeneration, the appearance of bizarre astrocytes, etc. The pathogenetic mechanism and predilection of the lesions described for peritumoral regions are discussed in light of recent radiobiologic information. (no Refs) (In ITA)

5. ANATOMO-TOMOGRAPHIC PARAMETERS OF CEREBRAL RADIONECROSIS FROM TREATMENT OF MALIGNANT GLIOMAS (MEETING ABSTRACT).

Soffietti R, Giordana MT, Milani R, Schiffer D, Sicuro L, Tarenzi L
Clinica Neurologica II, Universita di Torino, Torino, Italy
Tumori; 67(2,SupplA):79 1981

Out of 45 brains belonging to patients who underwent surgery for malignant glioma and were treated with radio- and chemotherapy, 7 had a clinicopathologic picture of delayed cerebral radionecrosis. In 6 cases the lesion was peritumoral and in 1 it was situated in the white matter of the contralateral hemisphere. Isodose curves were calculated for coronal histologic sections in each case by point to point reconstruction of horizontal and serial computerized axial tomography sections. Such an evaluation demonstrated that the areas of radionecrosis had received a radiation dose equal to or slightly higher than the tumor. It should be pointed out that there were areas which received an even higher radiation dose and did not display radionecrosis. This shows the importance of the peritumoral site in the etiology of radionecrosis and the problem of its differentiation from a recurrence. (no Refs) (In ITA)

6. HEMISPHERIC SUPRATENTORIAL ASTROCYTOMAS IN CHILDREN. LONG-TERM RESULTS IN 29 CASES.

Mercuri S, Russo A, Palma L
Instituto di Neurochirurgia, Universita di Roma, Viale dell'Universita 30/A, 00185 Rome, Italy
J Neurosurg; 55(2):170-173 1981

In a series of 41 cases of hemispheric supratentorial astrocytoma (HSA) in children, 29 patients have been followed for periods ranging from 5 to 27 yr. The follow-up data show that HSA's are relatively benign tumors. Twenty-two patients (76%) are still living: 12 in good, 8 in fair, and 2 in poor neurological condition. Their mean survival is 13.3 yr. Five patients died from tumor recurrence within 4 yr of the operation. All five were operated on before the age of 8 yr. The best results in terms of mean survival and quality of life were obtained in cases of cystic HSA, especially the pilocytic variety. In children, HSA tends to take the cystic form (often pilocytic), and its relatively benign course points up an analogy between this rare supratentorial tumor and the more common tumor of the cerebellum (the so-called 'cerebellar astrocytoma'). (Author abstract) (19 Refs)

7. OPTIC GLIOMA IN CHILDREN. A RETROSPECTIVE STUDY OF 57 CASES TREATED BY IRRADIATION.

Kalifa C, Ernest C, Rodary C, Sarrazin D, Bloch-Michel E, Lemerle J
Service de Pediatrie, Institut Gustave-Roussy, rue Camille Desmoulins, 94800 Villejuif, France
Arch Fr Pediatr; 38(5):309-313 1981

The treatment of 57 children (26 males, 31 females; 9 mo-15 yr old) with optic gliomas is described. Of the 57 patients, 30 had neurofibromatosis. Of the 57 patients, 55 presented with visual disorders, 5 with endocrine disorders, and 27 had increased intracranial pressure. Type I gliomas were observed in 3 patients, Type II in 18, and Type III in 36. Twenty-five were operated upon (usually for exploratory purposes) but all 57 patients underwent radiotherapy with 50-60 grays. Of the 57 patients, 42 were alive at 2-19 yr, although 20 were blind and 26 showed signs of significant mental retardation. (21 Refs) (In FRE)

NEURONAL CELL AND PRIMITIVE BIPOTENTIAL PRECURSOR CELL TUMORS

8. THE ROLE OF CELL KINETICS AND CYTOSTATICS IN CELL PROLIFERATION - SENSITIVITY TEST FOR NEUROBLASTOMAS, RECURRENT TUMORS AND TUMOR METASTASES.

Willnow U
Klinik und Poliklinik fur Kinderchirurgie, Karl-Marx Universitat, Bereich Medizin, Oststr, 21-25, DDR-705 Leipzig, E. Germany
Z Kinderchir; 33(2):110-121 1981

Tumors of the same histotype develop different degrees of malignity, and their reaction to the same therapy is different. The growth rate of 13 neuroblastomas, 6 assorted recurrent tumors and 7 metastases were studied in vitro on parts of biopsy material or resected tumors. The cell kinetic parameters using 3H-thymidine markers, DNA synthesis, mitotic rate and mean cell cycle rate were measured with automated radiographic techniques. The growth fraction can be calculated only approx. The neuroblastomas grew fast, the cell-cycle periods were 13.1-266.3 hr with an av of 71 hr. The recurrent tumors varied from decrease to acceleration. The fastest growing tumors were th lung metastases of Wilm's tumors and osteosarcomas. The cell cycle period was 13.0-87.0 hr with an av of 37.7 hr. All tumors have distinctly individual proliferation pattern. These cell kinetic parameters were used to monitor the sensitivity of the tumor cells to irradiation and cytostatic drugs and are expressed as 'cell-kinetic therapeutic index'. The use of the cell-kinetic patterns and the sensitivity data in clinical practice are discussed. (24 Refs) (In GER)

9. MULTIDISCIPLINARY TREATMENT OF MEDULLOBLASTOMA: A 5-YEAR EXPERIENCE WITH THE SIOP TRIAL.

Gerosa MA
Istituto di Neurochirurgia, Universita di Padova, 35100 Padova, Italy
Childs Brain; 8(2):107-118 1981

Treatment of 33 children with posterior fossa medulloblastoma were treated with the SIOP (Societe Internationale d'Oncologie Pediatrique) brain tumor regimen consisting of major surgical resection, extensive irradiation (5,000-5,500 R to the tumor, 3,500-4,000 R to the whole brain, and 3,000-3,500 R to the spinal cord), and combined chemotherapy with vincristine (1.0 mg/square meter (m2) for induction and 1.5 mg/m2, iv, weekly for a total of 8 courses over approx 48 wk) and lomustine, (100 mg/m2, po/wk for 8 wk over approx 48 wk). Of the 30 evaluable patients, 28 were still alive, with a mean actuarial survival of approx 28 mo. Of the survivors, the performance status was usually good (71.4% over 80 points). The rate of incidence of spinal lesions from radiotherapy was high: 32.1% of altered sitting-standing index, 25% of kyphoscoliosis. Endocrine deficiency was present in 14.3% of the patients. Mental or visual deficits, or the involvement of a cranial nerve, were not unusual. Cerebellar impairment was frequent. Leukopenia and thrombocytopenia were frequent and sometimes severe. Mild, transient liver toxicity occurred in nine cases, and four patients complained of signs and symptoms of toxic hepatitis. (30 Refs)

10. RADIATION TREATMENT FOR MEDULLOBLASTOMA: A 21-YEAR REVIEW.

Berry MP, Jenkin RD, Keen CW, Nair B, Simpson WJ
(c/o Jenkin), Ontario Cancer Foundation, Toronto-Bayview Clinic, 2075 Bayview Ave., Toronto, Ontario M4N 3M5, Canada
J Neurosurg; 55(1):43-51 1981

One hundred and twenty-two patients with medulloblastoma received postoperative irradiation at the Princess Margaret Hospital, Toronto, from 1958 to 1978, inclusive. The surgical procedure in these patients was total resection (44 patients), subtotal resection (66 patients), or biopsy alone (12 patients). Twenty-five patients received adjuvant chemotherapy. Overall 5-and 10-yr survival rates were 56% and 43%, respectively. Improved survival rates were associated with an increased degree of resection and with posterior fossa radiation doses of 5,200 rads or more. The posterior fossa was the common site of first relapse (in 56 patients, 46%). Systemic metastases at first relapse occurred in 18 of 52 patients (35%), and were associated with the use of ventriculosystemic shunts. Millipore filters did not prevent systemic relapse in shunted patients. A subset of 15 patients who received a posterior fossa dose of 5,200 rads or more after a total resection had a 5-yr survival rate of 77%, which remained constant to 10 yr. This result is considered to be the upper limit that can be achieved by current treatment methods. (Author abstract) (30 Refs)

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11. THE MORTALITY IN CHILDREN WITH NEUROBLASTOMA - THE TWO 10 YEAR STUDIES FROM THE DEPARTMENT OF PEDIATRIC ONKOLOGY OF THE TUBINGEN UNIVERSITY ARE COMPARED.

Kolb HJ, Schweizer P, Treuner J, Teufel U
Chirurgische Klinik der Hannoverschen Kinderheilanstalt, Ellernstrasse 40, 3000 Hannover 1, W. Germany
Z Kinderchir; 33(2):99-109 1981

The neuroblastomas are rare (1:10,000) in children under 14 y, but their mortality is very high 50-80% as reported in the literature. During the 10 y period (1960-1969) the mortality in our department was 72%, in the 25 patients treated, but in the following 10 y period (1970-1979) it decreased to 38% in the 32 patients treated. This remarkable decrease was mostly due to early diagnosis, which influences favorably all other prognostic parameters: age, stage (Evans), site of the primary tumor, histologic differentiation, postoperative excretion of metabolic catecholamines and how radical and complete was the removal of the tumor. This last parameter is the most important therapeutic factor and it could be sufficient, if prognostic factors like age (first yr of life) and Stage (I or II) are favorable. The radiotherapy and the cytotoxic treatment prolong the survival time and rate, the authors suggest reporting more variable survival time instead of the conventional 2 y survival time. (42 Refs) (In GER)

12. CONGENITAL NEUROBLASTOMA, NEUROBLASTOMA IN SITU, AND THE NORMAL FETAL DEVELOPMENT OF THE ADRENAL.

Ikeda Y, Lister J, Bouton JM, Buyukpamukcu M
(c/o Lister) Univ. Liverpool, Dept. Pediatric Surgery, Alder Hey Children's Hosp., Eaton Rd., Liverpool, L12 2AP, England
J Pediatr Surg; 16(4,Suppl1):636-644 1981

In normal fetal development nodular collections of neuroblast cells were found in the adrenal glands from 7 wk gestation; these nodules increased in size and number, and in all specimens from fetuses of 14-18 wk gestation, aggregates of nodules closely resembling neuroblastoma in situ could be found. From about 12 wk gestation the large neuroblast nodules appear to split up into smaller nodules and differentiation into chromaffin cells takes place. The mean nuclear size of neuroblasts at all stages of development studied was 4.25 +-0.84 microns, statistically significantly less than the mean nuclear size of the cells measured in seven neonatal neuroblastomas. Measurement of nuclear size may be a way of distinguishing a true potentially malignant neuroblastoma in situ from a normal benign residual neuroblast nodule. (Author abstract) (22 Refs)

MESODERMAL TUMORS OF THE CNS

13. CHARACTERISTICS OF INTRACRANIAL MENINGIOMAS IN CHILDHOOD.

Sano K, Wakai S, Ochiai C, Takakura K
Dept. Neurosurgery, Univ. Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113, Japan
Childs Brain; 8(2):98-106 1981

Eighteen cases of meningiomas in children less than 15 yr of age at the onset of symptoms are reviewed with respect to incidence, age and sex distributions, symptoms and signs at the onset, tumor locations, histological types, presence of cyst, dural attachments, and prognosis. These results were then compared with those of cases in adolescence (18 cases) and those in adults (498 cases). The distinct features of childhood meningiomas were a relatively high incidence in the lateral ventricles (11.1%), a high incidence of cyst formation in the tumor (16.7%), and a high incidence of cases without any dural attachment (12.5%). In both the childhood group and the adolescent group, males were predominant, while females predominated in adult meningiomas. The most common histologic type was the sarcomatous type (33.3%). Three of these cases were alive for more than 10 yr. (12 Refs)

14. MULTIPLE MENINGIOMAS EVALUATED BY COMPUTED TOMOGRAPHY.

Lusins JO, Nakagawa H, Connolly ES
65 East 79th St., New York, NY, 10021
Neurosurgery; 9(2):137-141 1981

The improvements of computed tomography in demonstrating multiple intracranial lesions, many asymptomatic, that were missed by previous diagnostic modalities was demonstrated in 15 patients with multiple meningiomas (13 females, 2 males; aged 30-88 yr). This represents an incidence of 8.9% among 168 consecutive cases of meningioma seen during the past 5 yr, which is significantly greater than the 1-3% previously reported. These 15 cases are briefly described. Possible reasons for the increased incidence and various theories of the etiology of multiple meningiomas are discussed. (18 Refs)

TUMORS OF THE CRANIAL AND SPINAL NERVE ROOTS

15. POSITIVE CONTRAST CISTERNOGRAPHY: ANALYSIS OF (1) FALSE NEGATIVE STUDIES, (2) FALSE POSITIVE DIAGNOSES OF ACOUSTIC NEUROMA.

Cooper PW
Dept. Radiology, Sunnybrook Medical Centre, 2075 Bayview Ave., Toronto, Ontario M4N 3M5, Canada
J Otolaryngol; 10(3):199-209 1981

In performing and interpreting positive contrast cisternograms, one must be aware that both false negative and false positive studies are possible. A false negative study is one in which the internal auditory canal is felt to be normally filled but in fact may not be. Reasons for this include inadequate views, misinterpretation of normal arachnoid extensions for the normally filled canal, jugular foramen, Meckel's cave, hypoglossal canal, and far lateral extension or wide cistern. False positive studies in which no acoustic neuroma is found at surgery can be subdivided into two groups on the basis of the positive contrast cisternogram: Group I is patients having cerebellopontine angle masses in which the canal may or many not fill, and Group II are patients with no significant angle mass but in which the canal does not fill normally with oil. (22 Refs)

16. PRIMARY SPINAL TUMORS IN INFANCY AND CHILDHOOD.

Giuffre R, Di Lorenzo N, Fortuna A
Inst. Neurosurgery, Rome Medical Sch., Rome, Italy
Zentralbl Neurochir; 42(2):87-98 1981

Of the 565 primary spinal tumors operated on at the Institute of Neurosurgery, Rome University Medical School up to December 1979, 61 (16 sympathetic tumors, 11 gliomas-ependymomas, 10 benign bone tumors, 9 sarcomas, 7 dysembryogenetic tumors, 4 neurinomas, 4 arachnoid cysts) were in children up to the age of 15 yr. Sixty percent were extradural and 40% intradural tumors. Distribution over the spinal column was uniform. The first 3 yr of life account for 34%. Motor deficits (86%), pain (63%) and sphincter disturbances (19%) were the most prominent complaints. The plain x-rays were abnormal in 65% of the patients, in a few cases permitting the identification of tumor type. CSF Protein was recorded in 50 patients and was abnormal in 42. Fifty-six patients had myelography and it was diagnostic in 55. CT-scan were performed in two patients and in both was diagnostic. Sixty-one patients had 63 neurosurgical interventions, the operative mortality being 1.6%. Ten patients required further surgery, retroperitoneal or mediastinal. Thirty-one patients received radiotherapy and 10 of these chemotherapy as well. Initial misdiagnosis and late referral to the neurosurgeon was common. Only 15 patients of this series presented minor neurological signs when first seen. And yet the longterm follow-up (mean 8.6 yr) in 43 cases shows that 77% of the patients lead a useful life. This prompts a less pessimistic attitude to the surgical treatment of spinal tumors in childhood. Microsurgical techniques permit today attempts at total removal even in intramedullary astrocytomas. To keep down the risk of post-treatment vertebral deformities it is important to limit laminectomy laterally and to insist on the wearing of an orthopedic jacket for the first few mo after operation. (Author abstract) (49 Refs)

SECONDARY TUMORS OF THE CNS

17. PITUITARY METASTASIS: INCIDENCE IN CANCER PATIENTS AND CLINICAL DIFFERENTIATION FROM PITUITARY ADENOMA.

Max MB, Deck MD, Rottenberg DA
(c/o Rottenberg) Dept. Neurology, Memorial Hosp., 1275 York Ave., New York, NY, 10021
Neurology; 31(8):998-1002 1981

In order to ascertain the incidence of pituitary tumors in cancer patients and to characterize the clinical presentation of pituitary metastases, the clinical experience with these tumors at Memorial Sloan-Kettering Cancer Center during the period 1976-1979 and a recent series of 500 consecutive autopsies in which the pituitary fossa and gland had been examined were reviewed. A search was made of the English language literature for pituitary metastases; the 28 cases (reported between 1914 and 1979) which included descriptions of clinical presentation and histologic proof of metastasis were recorded. In the clinical series, 4/5 patients had symptomatic pituitary tumors; histologic diagnosis was made in three of the cases (2 adenoma, 1 metastasis). Autopsy information yielded 18/500 (3.6%) metastases and 9/500 (1.8%) adenomas; all cases had been asymptomatic pituitary tumors, and skull films performed in 15 of the patients had given no evidence of tumor. In general, radiologic evaluation did not reliably distinguish metastasis from adenoma, but the clinical syndromes were distinctive. First symptoms and signs usually point to the diagnosis. Metastases present with diabetes insipidus (DI) or less commonly with oculomotor palsies. These symptoms occur in fewer than 2% of patients with pituitary adenoma. Visual loss and anterior pituitary insufficiency, characteristic of pituitary adenoma, are infrequent initial symptoms of metastasis but may follow DI. The differentiation between pituitary metastasis and adenoma may affect therapy. (32 Refs)

18. INCREASE OF BETA-ENDORPHIN IN CEREBROSPINAL FLUID AFTER REMOVAL OF ACTH-SECRETING PITUITARY ADENOMAS.

Furui T, Kageyama N, Kuwayama A, Nakao K, Fukushima M
Dept. Neurosurgery, Nagoya Univ. Sch. Medicine, 65 Tsurumai-cho, Showa-ku, Nagoya 466, Japan
Pain; 11(1):127-132 1981

Beta-endorphin (BEN) and met-enkephalin (MEK) were measured in cerebrospinal fluid (CSF) before and after removal of an ACTH-secreting pituitary adenoma in four patients with Cushing's disease. BEN was measured by radioimmunoassay, MEK was measured by radio-receptor assay, and ACTH in the plasma was measured by radioimmunoassay. After tumor resection, the ACTH level in plasma markedly decreased from 82.6 +-22.7 picog/ml to 16.7 +-4.1 picog/ml. The immunoreactive BEN level in CSF was significantly elevated after resection from 32.0 +-4.5 picog/ml to 61.8 +-10.7 picog/ml. In three cases, MEK-like substance level in CSF decreased after tumor resection, but the alteration was not statistically significant. These results suggest the possibility that BEN participates in the analgesic effect of hypophysectomy. (29 Refs)

19. SERUM PROLACTIN IN PATIENTS WITH HYPOTHALAMUS AND PITUITARY DISORDERS.

Lundberg PO, Osterman PO, Wide L
Dept. Neurology, Univ. Hosp., S-750 14 Uppsala, Sweden
J Neurosurg; 55(2):194-199 1981

Serum prolactin concentrations were studied in 115 patients with anatomically defined disorders in the hypothalamo-pituitary region. Fifty of the patients had expansively growing pituitary adenomas; in 17 of them (13 females and 4 males) the prolactin values were slightly raised (15 to 100 ug/liter), and in 13 (11 females and 2 males) they were over 100 ug/liter. The frequency of elevated prolactin values was higher for females than for males. Fifteen patients with invasively growing pituitary adenomas had very high serum prolactin levels (range 1,230 to 31,500 ug/liter, geometric mean 3,150 ug/liter). In a single case of malignant pituitary adenoma, the serum prolactin was at the lower level of detection. Of 49 further patients with suprasellar meningiomas, craniopharyngiomas, or other expansive or destructive lesions of the hypothalamus and sellar region, 15 had slightly raised prolactin values (max 114 ug/liter). Eight of these 49 patients had sellar destruction, with a roentgenological picture similar to that in patients with invasive pituitary adenomas. Among these eight patients, the max prolactin value was 67 ug/liter. It is concluded that moderately raised serum prolactin values (up to 100 ug/liter) in a patient with a sellar tumor does not prove that the tumor is a prolactinoma. A serum prolactin value of 100 to 1,000 ug/liter strongly indicates a prolactin-producing tumor. In a patient with sellar destruction, a serum prolactin value of over 1,000 ug/liter is proof that the destruction is caused by an invasive pituitary adenom a. (Author abstract) (22 Refs)

20. 24-HOUR PROLACTIN SUPPRESSION AND PITUITARY TUMOR SHRINKAGE BY PERGOLIDE (MEETING ABSTRACT).

Kleinberg DL, Greising J, Ragavan V, Seltzer T, Kricheff I, Kupersmith M, Flamm E
Department of Medicine,, New York Veterans Administration and New York University Medical Centers, New York, NY, 10010
63rd Annual Meeting of the Endocrine Society, June 17-19, 1981, Cincinnati, Ohio. The Endocrine Society 385 pp., 1981.

This report presents evidence that pergolide significantly inhibits human prolactin (hPRL) in hyperprolactinemic patients and also reduces the size of hPRL-secreting pituitary tumors. Fifteen patients most of whom had pituitary tumors with elevated hPRL were treated with pergolide. The initial doses of 50 ug in 14 patients and 100 ug in a 15th effectively lowered hPRL in 14 of them to a nadir of 32 ng/ml ranging from 1-7,600 ng/ml. This mean reduction to 18.6% of the pre-drug prolactin concentrations occurred at from 8 to 24 hr after administration. By 24 hr the mean hPRL was 26.3% of control. Eventual chronic doses of pergolide ranged from 50 to 400 ug. hPRL was normalized in 11 patients and significantly reduced in the other 3 continued on pergolide. Menstrual and sexual function improved in a majority. Five patients had repeat 24 hr studies on higher doses and suppression was found to be relatively uniform. At this time 6 patients have had both baseline and follow-up 4th generation computerized axial tomography scans from 2 to 6 mo after starting treatment. In 4 there was marked reduction in tumor size and in a 5th slight shrinkage or necrosis was noted. In the 2 with marked suprasellar extension the reduction in tumor vol was greater than 70%. Visual fields improved in 1 after a few wk. The 6th patient had an empty sella and there was no radiographic change. Thus, like bromocriptine, pergolide inhibits hPRL in hyperprolactinemic patients, restores sexual function and inhibits pituitary tumor size, but is more potent and has a longer duration of action. An antitumor effect of pergolide has been noted in all patients with tumors so far tested. (no Refs)

21. DELAYED RETURN OF HYPERPROLACTINEMIA AFTER BROMOCRIPTINE THERAPY IN WOMEN WITH PITUITARY PROLACTINOMAS (MEETING ABSTRACT).

Maxson W, Dudzinski M, Hammond C
Division of Reproductive Endocrinology, Duke University Medical Center, Durham, NC, 27710
63rd Annual Meeting of the Endocrine Society, June 17-19, 1981, Cincinnati, Ohio. The Endocrine Society 385 pp., 1981.

In this study chronic bromocriptine therapy was discontinued in 6 women with hyperprolactinemia who had been treated with bromocriptine (5-20 mg daily) for 5-14 mo. Plasma prolactin (PRL) concentration (conc) were determined every 4 hr for 48 hr and at 16 intervals over the next 60 days. Three of the women had histologically proven pituitary tumors (1 macroadenoma, 2 microadenomas) following transsphenoidal resection with persistent elevations of plasma PRL conc postoperatively, and 3 patients had marked sellar erosion on thin section tomography consistent with a diagnosis of adenoma. On bromocriptine the macroadenoma patient decreased her plasma PRL conc from 2085 to 77 ng/ml and the other 5 decreased their plasma PRL conc from 156.6 to 16.8 ng/ml. In the patient with the macroadenoma, plasma PRL conc began to increase within 12 hr after the last bromocriptine dose, reaching a max of 970 ng/ml at 49 days. In the remaining 5 patients, plasma PRL conc did not rise above 25 ng/ml until 1-9 days. The conc then gradually increased in all patients to a max at 23.4 days which was 151-528% greater than pretreatment conc in 3 patients and 46-84% less in 3 patients. Following peak conc, PRL thereafter decreased in all 5 women, reaching a plateau in [illegible] that was 8.1-83.1% pretreatment values. In 2 of these patients, the PRL conc was below 25 ng/ml at the end of the study, while in one patient the PRL had risen slightly (128% of pretreatment levels). These studies indicate that bromocriptine has a long-term effect on plasma PRL conc which is considerably longer than the plasma half-life of 3.1 hr. Because of the highly inconsistent pattern of plasma PRL response during the first 60 days after discontinuation of bromocriptine, decisions regarding tumor activity based on PRL conc should not be made within at least 2 mo after the discontinuation of the drug. (no Refs)

22. SURGICAL TREATMENT OF PITUITARY PROLACTINOMAS: POSTOPERATIVE PROLACTIN AND FERTILITY IN SEVENTY PATIENTS.

Landolt AM
Dept. Neurosurgery, Univ. Hosp., Ramistrasse 100, 8091 Zurich, Switzerland
Fertil Steril; 35(6):620-625 1981

The surgical results obtained in 70 patients with pituitary prolactinomas indicate that the success of surgery depends on the preoperative prolactin level and the diameter of the adenoma, and that the former is the more influential factor. Assessment of both of these parameters affords a good prediction of the endocrine result. The cure rates for different patient groups ranged from 4% to 90%. Postoperative results in women (57% with normal prolactin levels) were better than those in men (17% with normal prolactin levels). Of 19 women who desired pregnancy, 11 (58%) achieved successful pregnancies; 1 woman became pregnant twice. In addition, one women had an extrauterine pregnancy and one suffered a spontaneous abortion. Five required additional bromocriptine therapy. The data were evaluated analytically (Author abstract) (22 Refs)

23. HYPOTHALAMIC, PITUITARY, AND THYROID DYSFUNCTION AFTER RADIOTHERAPY OF HEAD AND NECK TUMORS (MEETING ABSTRACT).

Samaan NA, Siekavizza J, Schultz P, Maor M, Sampiere VA, Cangir A, Jesse RH
Departments of Medicine, Radiotherapy, Physics, Pediatrics and Surgery, The University of Texas System Cancer Center, M. D. Anderson Hospital and, Tumor Institute Houston, TX, 77030
Long Term Normal Tissue Effects of Cancer Treatment, April 13-15, 1981, Bethesda, Maryland Committe for Radiation Oncology Studies; 1981

We studied 110 patients with nasopharyngeal cancer and paranasal sinus tumors, who were free of the primary disease, one to 26 yr following radiotherapy. There were 65 males and 45 females. They were four to 75 yr of age with a mean of 36.5 yr. During therapy, both the hypothalamus and the anterior pituitary gland were in the field of irradiation. The dose of radiotherapy to the hypothalamus and the anterior pituitary gland was estimated to be 2,000 to 10,000 rads. In presence of lymph node metastasis, the larynx was shielded in some patients and the neck was irradiated, thus shielding the thyroid isthmus, but the thyroid lobes received 2,000 to 8,800 rads. We found evidence of a hypothalamic lesion in 71 patients, and an anterior pituitary lesion in 39. Sixty-one of the 110 patients received radiotherapy to the neck region for treatment of lymph node metastasis, and 22 developed hypothyroidism. Hyperprolactinemia in absence of radiological changes in the sella turcica was found in 62 patients indicating destruction of the prolactin inhibitory center. One young adult female, who developed galactorrhea and amenorrhea two yr following radiotherapy and also showed a high serum prolactin level but normal anterior pituitary function and sella turcica, regained her menses and a normal pregnancy following Bromocriptine therapy. These results indicate that endocrine deficiencies after radiotherapy of tumors of head and neck are common and should be detected early and treated. Long-term follow-up of these patients is indicated since complications may appear yr after the completion of radiotherapy and the patient may die of endocrine deficiencies in spite of the cure of the primary disease. However, endocrine deficiency may be an acceptable consequence of treatment for a potentially fatal disease. (no Refs)

24. ABSCESS FORMATION WITHIN PITUITARY TUMORS (MEETING ABSTRACT).

Nelson PB, Martinez AJ
Departments of Neurosurgery and Neuropathology, University of Pittsburgh, Pittsburgh, PA, 15213
63rd Annual Meeting of the Endocrine Society, June 17-19, 1981, Cincinnati, Ohio. The Endocrine Society 385 pp., 1981.

Three consecutive cases are presented where pituitary abscesses were found within pituitary tumors. All tumors were large and all patients had evidence of pituitary insufficiency. In two of the cases the abscesses were found three yr and four mo consecutively following transsphenoidal surgery for nonhormonal secreting chromophobe adenomas. In the third case a pituitary abscess was found in a previously undiagnosed nonhormonal secreting chromophobe adenoma. In all cases, the diagnosis was made preoperatively and the patients were begun on stress doses of hydrocortisone and antibiotics prior to surgery. Two patients underwent transsphenoidal drainage of the abscess and one patient underwent transcranial decompression of the tumor with drainage of the abscess followed by a second transsphenoidal drainage of the abscess. Bacteroides, coagulase positive staphylococcus, and corynebacterium striatum were cultured in each of the three cases respectively. All patients were treated with six wk of parenteral antibiotics. The three patients recovered with minimal neurological deficits. The constant finding in the three cases included headache, fever, visual disturbance, enlarged sellae, colony stimulating factor (CSF) pleocytosis, and negative CSF cultures. Meningeal signs were only present in one of the patients. Abscess formation within pituitary adenomas presumably is secondary to contamination by sphenoid sinus flora after the tumor has eroded into the sinus or operative contamination. Early suspicion of the diagnosis based on the above clinical findings with early treatment with antibiotics and operative drainage appears to be important in decreasing the mortality and morbidity. (no Refs)

25. PRIMARY AMENORRHEA AND PITUITARY ADENOMAS.

Coulam CB, Laws ER, Abboud CF, Randall RV
Dept. Obstetrics and Gynecology, Mayo Clinic, 200 First St. S.W., Rochester, MN, 55905
Fertil Steril; 35(6):615-619 1981

From 1972 to 1980, 210 patients underwent transsphenoidal operation for removal of a prolactin-secreting tumor. Eight of the patients had primary amenorrhea. All eight patients had had a normal thelarche and pubarche without menarche, and all eight had hyperprolactinemia and abnormal findings on sella turcica tomography. After operation, only one patient did not have persistent hyperprolactinemia, and this patient was the only one who began spontaneous menses. The data indicate that, although prolactin hypersecretion interferes with menstrual function, it does not alter other pubertal development and that, if the source of the excessive prolactin can be removed, the removal alone may initiate spontaneous menses. In this report, however, patients with prolactin-secreting adenomas and primary amenorrhea had a high incidence of persistent hyperprolactinemia after operation (seven of eight patients). (Author abstract) (21 Refs)

OTHER THERAPY OF CNS MALIGNANCIES

26. CHEMOTHERAPY OF PEDIATRIC BRAIN-STEM TUMORS.

Fulton DS, Levin VA, Wara WM, Edwards MS, Wilson CB
(c/o Levin) Brain Tumor Res. Center, 783 HSE, Univ. California, San Francisco, CA, 94143
J Neurosurg; 54(6):721-725 1981

Forty-five children harboring brain-stem tumors were treated at the University of California, San Francisco, between 1969 and 1979. Pathological diagnoses were made in 19 patients. All patients received radiation therapy (RT). Thirteen patients received chemotherapy before, during, or immediately after RT. Twenty-four patients were treated with chemotherapy at the time of tumor progression, after initial treatment with RT alone. No statistically significant difference in time to tumor progression or survival was found for treatment with chemotherapy as an adjuvant to RT compared to treatment with RT alone followed by chemotherapy administered at the time of tumor progression. There were, however, more long-term survivors in the group that was first treated with chemotherapy at the time of tumor progression. There was no statistically significant correlation between survival and tumor pathology or location, although there were more long-term survivors among patients harboring low-grade gliomas and among patients with tumors confined to the midbrain. The authors documented the response of some brain-stem tumors to chemotherapy; however, cooperative controlled studies will be required to determine the optimum treatment for this disease. (Author abstract) (17 Refs)

27. EFFECT OF RADIOTHERAPY OF TUMORS IN THE BRAIN STEM: EXAMINATION BY MEANS OF PICTURES OF COMPUTERIZED TOMOGRAPHY (CT) (MEETING ABSTRACT).

Nakamura S, Nishimoto H, Ohata H, Tsubokawa T, Moriyasu N
Dept. Neurosurgery, Nihon Univ., Sch. Medicine, Itabshi-ku, Tokyo 173, Japan
Proceedings of the 4th Annual Meeting of the Japanese Society of CNS Computerized Tomography held in Tokyo, 17-19 January, 1981. The Japanese Society of CNS Computerized Tomography, Tokyo 173, Japan, 146 pp., 1981.

The effect of radiotherapy was examined in 16 patients in whom tumors occurred in the brain stem or the neighboring area and whose tumor pictures seen on CT were clearly reduced by radiotherapy. For the therapy, a total of 2,650 to 6,150 rad of Co60 was given. The tumor picture on plain CT was reduced without change in density, but there was no case in which the density increased. Decrease of contrast enhancement was recognized in 10 of the 16 cases. In 12 of 15 cases in which perifocal low density (PFLD) was seen, there was a marked reduction or disappearance of PFLD, but in the remaining 2 cases PFLD was not reduced and reduction of the tumor itself also was slight. There was one case of medulloblastoma in which reduction of PFLD was not seen although the tumor was reduced very markedly. (no Refs) (In JPN)

OTHER CLINICAL ASPECTS OF CNS CANCER

28. CHANGES IN INTELLECT AND IQ FOLLOWING COMBINED TREATMENT TO THE BRAIN (MEETING ABSTRACT).

Meadows AT, Gordon J, Littman P, Fergusson J, Moss K

Departments of Pediatrics, Phychiatry and Radiation Therapy, University of Pennsylvania School of Medicine, Philadelphia, PA

Long Term Normal Tissue Effects of Cancer Treatment, April 13-15, 1981, Bethesda, Maryland Committe for Radiation Oncology Studies; 1981

Newly diagnosed children with acute lymphocytic leukemia (ALL) who had achieved remission were tested prior to receiving radiotherapy (RT). They were retested 1-2 yr later and then 3-4 yr after that with the testing session including measures of other neuropsychologic functions. All of these children had been treated with 2400rad cranial RT, 6 doses of intrathecal methotrexate (MTX) and oral MTX along with the usual other agents for 3 to 5 yr. No major significant changes were noted between the first and second testing, but large differences, which could not be explained by chance or by the standard error of measurement of the tests, were seen after 3-4 yr. 12/18 children for whom 3 tests were available showed significant declines in IQ (10 or more IQ points). Those who declined were more likely to be younger than 6 yr at diagnosis and there appeared to be no relationship between duration or intensity of therapy and degree of reduction in IQ score. When other neuropsychologic functions were examined, a large proportion of the group were impaired in: visual perception and visual motor integration and several aspects of memory (visual and auditory sequence and auditory verbal). Four children with ALL who had received similar therapy, including intrathecal MTX but no RT, were tested many yr after diagnosis and none was found to have deficits. We speculate that these low doses of RT may be insufficient to cause normal brain tissue damage but they result in permeability changes in blood vessels. (no Refs)

SELECTED PRECLINICAL ASPECTS OF CNS CANCER

29. GROWTH AND CHEMOTHERAPEUTIC RESPONSE IN ATHYMIC MICE OF TUMORS ARISING FROM HUMAN GLIOMA-DERIVED CELL LINES.

Bullard DE, Schold SC, Bigner SH, Bigner DD

(c/o Bigner), Duke Univ. Medical Center, P.O. Box 3156, Durham, NC, 27710

J Neuropathol Exp Neurol; 40(4):410-427 1981

Fifteen permanent cell lines derived from human gliomas were sc transplanted into athymic nude mice (nu/nu genotype, NIH Swiss and BALB/c backgrounds). Four were tumorigenic. Three of the four (D-54 MG, U-118 MG, and U-251 MG) produced progressively growing, solid, noncystic tumors. Sc vol measurement of these tumors, which correlated directly with tumor wt, was a reliable method for monitoring growth. All three cell lines which produced progressively growing sc tumors were also tumorigenic when cells were inoculated intracerebrally. These grew as well-circumscribed, intraparenchymal brain tumors. After initial implantation, each of the progressively growing, solid, sc tumors was histologically similar to the permanent cell lines from which it was derived. Tumors could be reliably passed, and stabilization of latency perio ds and growth rates developed. Tumors became morphologically less distinct in later passages, though some individual features remained. Mice bearing sc tumors from each of these cell lines were treated with a single ip dose of 25 mg/kg BCNU and compared to controls receiving only drug vehicle. A significant, but different, amount of reduction in tumor mass occurred among each of the three tumor lines. This model allows cell lines derived from human gliomas to be grown in animal hosts, thereby providing a potential means for evaluating growth parameters and chemotherapeutic responsiveness of tumors derived from individual human gliomas or cell lines. (Author abstract) (28 Refs)

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NEUROGLIAL CELL TUMORS

1. RELIABILITY OF COMPUTED TOMOGRAPHY IN ASSESSING HISTOPATHOLOGICAL FEATURES OF MALIGNANT SUPRATENTORIAL GLIOMAS.

**Lilja A, Bergstrom K, Spannare B, Olsson Y
Dept. Diagnostic Radiology, Univ. Hosp., S-750 14 Uppsala, Sweden**

J Comput Assist Tomogr; 5(5):625-636 1981

A new method was developed whereby close comparisons can be made between components of a computed tomography

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(CT) image and neuropathological findings. This was achieved by a combination of intravital (terminal) CT, postmortem CT, and whole brain sectioning of formalin-fixed tissue. The method was applied in seven cases of malignant supratentorial astrocytic gliomas (Kernohan Grades III and IV) and in one case of thalamic ependymoma. The glioblastoma-like parts of the astrocytic gliomas were usually correctly delineated by postcontrast CT, although there were exceptions to this rule. Tumor components consisting of diffusely growing malignant astrocytoma were difficult or impossible to delineate by CT. Necrotic areas within the tumors were accurately outlined by postcontrast CT. Peritumoral edema was correctly delineated by CT, but growth of diffuse astrocytoma or the presence of astrocytic gliosis within this edematous area seems difficult or impossible to evaluate by current CT techniques. (Author abstract) (28 Refs)

2. INTRA-ARTERIAL BCNU CHEMOTHERAPY FOR THE TREATMENT OF MALIGNANT GLIOMAS OF THE CENTRAL NERVOUS SYSTEM: A PRELIMINARY REPORT.

Greenberg HS, Ensminger WD, Seeger JF, Kindt GW, Chandler WF, Doan K, Dakhil SR
Dept. Neurology, Univ. Michigan Medical Sch., Ann Arbor, MI, 48109
Cancer Treat Rep; 65(9):803-810 1981

We treated six patient with unilateral malignant astrocytomas with pulse doses of ia carmustine (BCNU) (200 mg/m2 initially, with escalating doses every 6-8 wk) via transfemoral selective internal carotid catheterization. Four patients had had partial resections without prior radiation therapy and received no steroids. They had decreased tumor stain and surrounding edema after two to four cycles of chemotherapy. For one patient, results of the neurologic examination returned to normal, with total disappearance of her tumor as assessed by computerized tomographic scan. Objective tumor response continued for 7 mo in three patients and for 3 mo in one. In two of the four patients, chemotherapy was discontinued because of retinal toxicity and not because of treatment failure. Two patients had had partial resections and radiation therapy. One patient had stable disease for 4 mo, and the second had progressive disease with gradual visual loss beginning in the infused eye 3 wk after the second treatment. The catheterization procedure is safe; it was without immediate complication in 17 BCNU infusions. In summary, high-dose ia BCNU is well-tolerated and is an effective initial chemotherapeutic modality. (Author abstract) (13 Refs)

NEURONAL CELL AND PRIMITIVE BIPOTENTIAL PRECURSOR CELL TUMORS

3. CHEMOTHERAPY OF ADVANCED NEUROBLASTOMA: DOES ADRIAMYCIN CONTRIBUTE?

Ninane J, Pritchard J, Malpas JS
(c/o Pritchard), Hosp. Sick Children, Great Ormond St., London WC1N 3JH, England
Arch Dis Child; 56(7):544-548 1981

Between 1970 and 1977, 69 children with newly diagnosed stage III or IV neuroblastoma were treated with pulses of either cyclophosphamide and vincristine (CV) (n = 23), or cyclophosphamide, vincristine, and adriamycin (CVA) (n = 46). The 'complete' and partial response rates were 35 and 22% to CV, and 43 and 26% to CVA. For 'complete' responders the median time to relapse was 18 mo for those treated with CV, and 17 mo for those treated with CVA; for partial responders the times were 5 and 7 mo respectively. At 2-1/2 yr only 17% of the CV patients and only 13% of the CVA patients were alive and free of disease, giving a 15% overall survival rate. The addition of adriamycin to cyclophosphamide and vincristine did not significantly improve the response rate, duration of response, or survival in these children with advanced neuroblastoma. The previously noted favorable effects of age less than 1 yr at diagnosis and of female sex were confirmed. The equally poor survival for Stage III and Stage IV patients justifies the inclusion of Stage III patients in a bad prognosis group. (Author abstract) (21 Refs)

4. NONSURGICAL TREATMENT OF INTRASPINAL NEUROBLASTOMA.

Molofsky WJ, Chutorian AM
Coll. Medicine and Dentistry of New Jersey, MSB H-510, 100 Bergen St., Newark, NJ, 07102
Neurology; 31(9):1170-1173 1981

Two male infants with myelographically documented intraspinal extension of neuroblastoma, but only minimal neurologic deficit, were successfully treated without laminectomy. In one patient myelogram revealed a left paraspinal mass with large extradural impression from T3-T6 and displacement of the spinal cord to the right. The mass was partially excised. Postoperatively the patient remained well and was treated with 800 rad to the tumor bed and spine. Studies at 4 mo were normal; at 10 mo the lumbar, thoracic, and cervical myelograms were normal. After 5 yr no abnormality was noted. In the second patient, various studies including skeletal survey and myelogram revealed a large retroperitoneal calcified mass, mainly on the right but with some extension to the left; involved areas included pedicles T9-T12 and extended from L1 through T9. Dexamethasone (DEX; 50 mg) was given before exploratory laparotomy. Laparotomy revealed a large mass originating in the paravertebral area in the chest, and extending through both diaphragms and across the midline beneath aorta, vena cava, pancreas, and both adrenals. The patient did well postoperatively; DEX was reduced gradually and polychemotherapy and a course of radiation were administered. After approx 3 mo examination was unremarkable; muscle tone in the legs was normal and myelogram gave no evidence of tumor. Chemotherapy was continued and approx 6 mo later the patient was free of neurologic abnormality. (19 Refs)

MESODERMAL TUMORS OF THE CNS

5. EFFECT OF RADIATION ON MENINGIOMA.

Yang D, Yang H, Zhang F
Dept. Neurosurgery, Huashan Hosp., Shanghai First Medical Coll., Shanghai, People's Republic of China
Zhonghua Shenjing Jingshenke Zazhi; 14(1):12-13 1981

Intracranial meningioma is a benign tumor which can generally be treated by surg ical removal. However, in some cases when it is located too close to vital structures or too widespread, resection is not possible. In such cases, opinions differ whether deep radiotherapy can be effective. This is the first report in China on radiotherapy of a case of angioblastic meningioma. The patient (male, aged 37 yr) presented with suspected glioma located at the motor region with abundant blood vessels. Infratemporal muscle surgery was performed to alleviate intracranial pressure, followed by telecobalt-60 therapy (total dosage 6,402 rads). Patient recovered and returned to work 1 yr after surgery. However, 4 yr after radiotherapy, patient was readmitted. Surgery and pathology revealed angioblastic meningioma with radiation reaction. Patient was well 3 mo after surgery. The value of radiotherapy in meningioma is discussed. (5 Refs) (In CHI)

TUMORS OF THE CRANIAL AND SPINAL NERVE ROOTS

6. THE ARGON LASER IN ACOUSTIC TUMOR SURGERY.

Glasscock ME, Jackson CG, Whitaker SR
1811 State St., Nashville, TN, 37203
Laryngoscope; 91(9,part1):1405-1416 1981

CO2 laser surgery has been employed successfully in the larynx for the past 10 yr. Because of the nature of the CO2 beam, it is necessary to mount the laser itself onto the operating microscope, thereby making it difficult to adapt to otologic microsurgery. The ability of the argon laser to be transferred through a fiber optic bundle has made it possible to introduce a whole new concept to microsurgery of the ear and adjacent structures. The argon laser has been used by the authors, on a routine basis, in all acoustic neuroma surgery for the past 10 mo (30 cases). The purpose of this paper is to present their preliminary experience. Surgical technique is covered in detail describing the many advantages the laser has provided in the management of these difficult lesions. (Author abstract) (7 Refs)

7. CHORDOMA.

Saxton JP
Dept. Radiotherapy, Univ. Texas System Cancer Center, M. D. Anderson Hosp. and Tumor Inst., Houston, TX, 77030
Int J Radiat Oncol Biol Phys; 7(7):913-915 1981

From 1948 to 1976 19 patients were treated for tumors diagnosed as chordoma; ages ranged from 4-80 yr, with 5 under 16 yr; 12 were male. Sites involved included 6 basisphenoid, 2 lumber spine, and 11 sacrococcygeal area. Four cases were treated by surgery only, six received radiation therapy (RT) only with doses of 4,000-6,500 rad, and nine received a combination of surgery plus RT with radiation doses of 3,500-7,000 rad. All those treated by surgery only died after survival times of 0-36 mo. All those receiving RT only also died, but survival times were much longer (4-60 mo). There was no correlation between dose and length of remission. Three of those receiving combined therapy are still alive after 36-80 mo. Those who died had survived for 5-51 mo. Palliation was greatest with combined therapy and poorest with surgery only. Determination of cure was difficult because of the slow progression of the disease. Results suggest that local tumor control can be achieved after resection of the obvious tumor mass by radiotherapy of up to 7,000 rad. Such high doses might produce the best results when given over a protracted period of time. (8 Refs)

8. CHORDOMA OF THE CERVICAL SPINE.

Murali R, Rovit RL, Benjamin MV, Sundaresan N, Odom GL
Dept. Neurosurgery, St. Vincent's Hosp. and Medical Center, 153 West 11 St., New York, NY
Neurosurgery; 9(3):253-256 1981

Eight cases of chordoma of the cervical spine, a rare tumor, are described. Combination of osteosclerosis and lysis, multiple vertebral involvement, and pre- or paracervical soft tissue mass were characteristic. Radiographic indications were minimal when neck pain was the only symptom. Tumors were partially excised using an anterior approach. The limiting factor to complete excision of the tumor was its dissemination in the epidural space and along the nerve root sheath. Bone grafts provided stability after removal of cervical bone. Radiation doses of 4,500 and 6,000 rad were given in two cases. Two patients died, one was lost to follow-up, and five are alive and well. Survival time has been as long as 46 yr after initial diagnosis. Repeated surgery using the anterior approach seems to be successful in palliating symptoms, although no cures were obtained. (7 Refs)

TUMORS OF THE CHOROID PLEXUS AND PINEAL REGIONS

9. PINEAL REGION TUMORS: COMPUTED TOMOGRAPHIC-PATHOLOGIC SPECTRUM.

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AJNR; 2(5):415-420 1981

The heterogeneity in both histopathologic and computed tomographic (CT) appearance was demonstrated in a series of 17 pineal gland tumors, 9 of which were proven by biopsy or autopsy. Included were 4 females (av age 27 yr) and 13 males (av age 15 yr). There were two germinomas, two teratocarcinomas and one each of pineal hamartoma, benign teratoma, astrocytoma, and neurilemmoma among the biopsy-proven cases. The other cases included one 'malignant pineal tumor', one pineal lipoma, five presumed germinomas, and one undiagnosed case. A presumptive histologic diagnosis on the basis of CT alone was not possible and benign and malignant tumors could not be differentiated. An exhaustive search for a suprasellar mass is imperative in all pineal region tumors. Other lesions that should be included in the differential diagnosis of pineal tumors include exophytic brainstem glioma, neurilemmoma, incisural meningioma, intraventricular craniopharyngioma, and metastasis, since these all appear as enhancing masses in or adjacent to the posterior third ventricle or quadrigeminal plate. Since biopsy is now feasible for pineal tumors, it is recommended for treatment planning. (21 Refs)

10. ASSESSMENT AND MANAGEMENT OF PINEAL-REGION AND RELATED TUMORS.

Wood JH, Zimmerman RA, Bruce DA, Bilaniuk LT, Norris DG, Schut L
Div. Neurosurgery, Emory Univ. Clinic, 1365 Clifton Road, NE, Atlanta, GA, 30322
Surg Neurol; 16(3):192-210 1981

Twenty-nine patients underwent computed tomographic (CT) evaluation of tumors either in or related to the pineal region. Preoperative CT scans accurately assessed tumor characteristics but could not precisely predict tumor type. Histological confirmation was obtained in 21 of 24 nonlipomatous tumors without mortality. Tissue diagnosis was essential in defining the goals of surgery (resection of symptomatic benign tumors or reduction of malignant tumor burden) and in determining the need for postoperative radiation or chemotherapy, or both. Surgical intervention did not increase the incidence of subarachnoid seeding. Most lipomas were incidental, whereas the epidermoid tumors and the benign teratomas were symptomatic and potentially resectable. Most pineal or germ-cell tumors and the majority of gliomas responded to either or both radiation or chemotherapy. Twenty-one of 24 patients with nonlipomatous tumors were clinically improved following treatment. Serial postoperative CT scanning documented two cases of tumor recurrence at the primary site despite prior CT evidence of resolution. CT scanning proved reliable but not infallible in evaluating treatment efficacy. (Author abstract) (80 Refs)

SECONDARY TUMORS OF THE CNS

11. THE PROLACTINOMA IN THE MAN. PREOPERATIVE EVALUATION OF 40 PATIENTS.

Somma M, Beauregard H, Rasio E
Service d'Endocrinologie, Hopital Notre-Dame, Montreal, Quebec, Canada
Neurochirurgie; 27(Suppl1):37-39 1981

The clinical and biological evaluation of 40 men (15-62 yr old) with biologically and surgically proven prolactinomas is described. A decrease in libido with sexual impotency was reported in 82.5% of the patients. Headache was observed in 45% patients. Visual field disorders accompanied optic nerve atrophy in 5/9 patients. Gynecomastia was observed in 9 patients, with galactorrhea in 6/9. Infertility was certain in 5/40 patients. Morphological hypogonadism was observed in 4/40 men. Radiological study showed that 8 patients had Stage I microadenomas, 26 had an enclosed Stage II adenomas, (12/26 with suprasellar enlargement), and 6 had invasive Stage IV adenomas (5/6 with suprasellar enlargement). In the 40 patients, base level prolactinemia ranged from 30 to 70 nanog/ml. Of the seven patients with hypopituitarism, one had partial thyroid stimulating hormone and ACTH deficiency, two had ACTH deficiency, and 4 exhibited hypopituitarism. Insulin resistance was found in 22 patients. A significant increase in prolactin was observed in only one patient. Cortisol levels were normal in 21 patients and decreased in 7. Growth hormone was normal in 15 patients and decreased in 7. In response to luteinizing hormone releasing hormone stimulation, follicle stimulating hormone was increased by greater than 100% in five patients and luteinizing hormone increased by more than 200% in six. No correlation was observed between the level of prolactinemia and patient age. The 17-beta-hydroxy-androgens were clearly decreased in the majority of the 19 patients in whom they were measured. (15 Refs) (In FRE)

12. PROLACTINOMA. SURGICAL ASPECTS.

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Neurochirurgie; 27(Suppl1):41-60 1981

The diagnosis and treatment of 355 patients (55 men, mean age of 39 yr; 300 women, mean age of 28 yr) with prolactinomas is described. The surgical technic employed is described. The classification of the prolactinomas observed in the 300 women and the presence or absence of suprasellar expansion is described. The sellar floor, dura mater, and venous sinus were intact in 97.3%, 95.6%, and 93.3% of the 300 patients, respectively. A tumor was found in 293/300 patients. The vol of the tumor was studied in relation to radiological stage and its visibility on the surface of the pituitary. In 260/300 cases, the tumor was grayish purple, in 20, milky white, and in 12, another color. Most (80%) of the tumors were soft, homogeneous, and easily detached in pieces with the curette or aspirator. Cysts or tumoral necrosis were observed in some patients. Suprasellar expansion was rare among the 300 women. The pituitary was normal in 230/300 women. Technical difficulties met during surgery are described. In 270/300 cases, the tumor was removed and verified by pathology. Postoperative complications and second interventions are described. Among the 275/300 patients in whom prolactin levels were measured during the 30 days following surgery, the prolactin levels were normal in 177. The 55 male patients with prolactinomas are described. Radiologically, 8 had Grade I sella turcica, 39 Grade II (18/39 with suprasellar expansion), and 8 Grade IV (5/8 with suprasellar expansion). The operative findings, postoperative complications, and surgical results are described for these men. Postoperative prolactin levels were normalized in 20/55 men. (13 Refs) (In FRE)

13. THE PROLACTINOMA IN THE MAN. THERAPEUTIC RESULTS IN 40 MEN.

Somma M, Beauregard H, Rasio E
Service d'Endocrinologie, Hopital Notre-Dame, Montreal, Quebec, Canada
Neurochirurgie; 27(Suppl1):91-94 1981

The immediate and long term biological and clinical results of surgery in 40 men with prolactinomas are described. In 15/40 men, blood prolactin levels were normalized in the immediate postoperative period. Of these 15 men, 8 had Stage I adenomas and 7 Stage II (3/7 with suprasellar expansion). All 15 patients had prolactin levels of less than or equal to 700 nanog/ml. Of the 25 patients whose prolactin levels were not normalized postoperatively, 19 had Stage II adenomas (9/19 with suprasellar expansion) and 6 had Stage IV adenomas (5/6 with suprasellar expansion). Of these 25 patients, 19 had prolactinemia of greater than 700 nanog/ml. Of the 15 patients, in whom prolactin levels were normalized following surgery, 14 regained their sexual function; only 1/15 required replacement hormone therapy for panhypopituitarism. Eighteen of the 25 patients with elevated postoperative prolactin levels were treated with bromocriptine. The response to this treatment is described. Two patients underwent a second operation. (9 Refs) (In FRE)

14. SECRETION OF LH, FSH AND PRL SHOWN BY CELL CULTURE AND IMMUNOCYTOCHEMISTRY OF HUMAN FUNCTIONLESS PITUITARY ADENOMAS.

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Clin Endocrinol (Oxf); 15(2):103-112 1981

Hormone secretion by ten functionless human pituitary adenomas in cell culture has been measured, and compared with tissue immunocytochemistry and electron microscopy, as well as results with a normal pituitary. Patients presented following routine x-ray and had no clinical or biochemical endocrine abnormality apart from one male with raised serum FSH and

PRL, normal LH, and low testosterone. Of the ten adenomas, nine secreted both LH and FSH in cell culture and five of these also secreted PRL, one did not secrete any anterior pituitary hormones (ACTH was not measured). No GH or TSH was detectable in the cultures of the nine LH/FSH secretors excluding the possibility of contamination by normal anterior pituitary. The normal pituitary cells secreted all anterior pituitary hormones; the amounts of FSH/LH being comparable with those of the adenomas. Immunostaining confirmed the cell culture results and showed the adenoma FSH/LH cells to be scattered singly or in small groups of two to five cells with both hormones usually being in the same cell. PRL where found was in separate cells. Hormone granules were small (50-160 nm), round or irregular and scattered in the cytoplasm of rounded cells of low secretory activity. The negatively staining cells were not different ultrastructurally to those staining positively. It is concluded that a significant proportion of functionless pituitary adenomas have detectable low levels of LH/FSH secretion often accompanied by PRL when examined by cell culture of immunocytochemistry. Although these adenomas were endocrinologically quiescent activity could have been masked because of postmenopausal secretion and one male probably had an FSH-secreting adenoma. (Author abstract) (32 Refs)

15. ABNORMAL REGULATION OF PROLACTIN SECRETION AFTER SUCCESSFUL SURGERY FOR PROLACTIN-SECRETING PITUITARY TUMOURS.

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Clin Endocrinol (Oxf); 15(2):165-174 1981

Patients with prolactin-secreting pituitary tumors have a diminished prolactin (PRL) response after administration of a variety of stimulatory agents, including thyrotropin-releasing hormone (TRH), chlorpromazine (CPZ) and insulin-induced hypoglycemia. We examined responses to these agents in 67 women with PRL-secreting tumors before and after transsphenoidal surgery. Twenty-nine of the women were cured as defined by restoration of normal serum PRL concentrations and resumption of regular menses. One yr following transsphenoidal surgery, patients with normal PRL concentrations and regular menses had normal PRL responses to TRH, while the responses to CPZ and insulin hypoglycemia were not improved. The reversible impairment of PRL response to TRH reflects suppressed function of normal PRL-secreting cells, and the persistence of abnormal PRL responses to provocative stimuli after successful tumor removal may reflect some fundamental defect in the regulation of PRL secretion in patients with PRL-secreting adenomas. When growth hormone (GH) reserve after insulin hypoglycemia was represented as the mean absolute increment above the basal concentration and compared with normal subjects, women with PRL-secreting tumors had a diminished response that returned to normal after successful surgery. This reversible impairment of GH secretion is not adequately reflected by standard criteria for GH response and suggests that PRL may have a role in the regulation of GH secretion. (Author abstract) (46 Refs)

16. THE INCIDENCE AND CLINICAL MANIFESTATIONS OF ACTH-PRODUCING PITUITARY ADENOMA AFTER BILATERAL ADRENALECTOMY FOR CUSHING'S SYNDROME ('NELSON'S SYNDROME').

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Schweiz Med Wochenschr; 111(37):1346-1352 1981

Twenty-nine out of 39 patients bilaterally adrenalectomized for pituitary-dependent Cushing's syndrome between 1958 and 1979 have been followed up at regular intervals. ACTH-producing pituitary adenomas were detected and removed in nine of them up to 1981. In four additional patients an enlarged sella turcica was already found at the time they had Cushing's syndrome, and therefore they were first treated by pituitary surgery or radiotherapy. In the adrenalectomized patients hyperpigmentation was the major clinical symptom of the adenoma. Only in three instances did extrasellar growth of the adenoma cause ophthalmoplegia or narrowing of the visual fields. The existence of intrasellar ACTH-producing microadenomas in five additional patients seems highly probable in view of hyperpigmentation, excessively elevated plasma ACTH concentrations and radiological evidence of sella deformations. These observations indicate that in patients adrenalectomized for pituitary-dependent Cushing's syndrome ACTH-producing adenomas are more common than previously assumed. Moreover, according to recent reports, ACTH-producing microadenomas are frequently found in pituitary-dependent Cushing's syndrome and are assumed by many clinical endocrinologists to be the primary cause of this disease. Therefore, bilateral adrenalectomy is no longer the undisputed therapy of first choice and it is necessary in each individual case to consider carefully whether an attempt to remove selectively an ACTH-producing pituitary adenoma by microsurgery might not be preferable. (Author abstract) (38 Refs) (In GER)

17. ACTH SECRETION FROM PITUITARY ADENOMAS OF CUSHING'S DISEASE IN VITRO.

Nakane T, Kuwayama A, Okada C, Watanabe M, Yoshida J, Kageyama N

Dept. Neurosurgery, Nagoya Univ. Sch. Medicine, Nagoya, Japan

Nippon Naibunpi Gakkai Zasshi; 57(3):270-281 1981

The autonomy of ACTH secretion in Cushing's disease was studied. Adenoma tissue explants from eight patients were placed in primary culture immediately after surgical removal. These explants secreted high levels of ACTH for as long as 1 mo. ACTH secretion by residual anterior pituitary tissue in Cushing's disease patients, as well as normal pituitary tissue showed a decrease to undetectable levels within 1 mo. Adenoma tissue was perfused with lysine-vasopressin. In seven of eight cases, ACTH secretion was induced. Little or no latency period was noted. No dose-response relationship was detected. Dexamethasone inhibited ACTH secretion in only one of four cases. Experimental results agree with clinical findings that selective adenectomy produces clinical improvement and a return to normal pituitary function, including normal diurnal rhythm. Autonomy of ACTH secretion apparently is derived from adenoma tissue in Cushing's disease. The primary lesion is evidently in the pituitary gland, rather than the hypothalamus. (39 Refs) (In JPN)

18. FOLLOW-UP STUDY ON TREATMENT IN 27 PATIENTS WITH CUSHING'S DISEASE: ADRENALECTOMY, TRANSSPHENOIDAL ADENOMECTOMY AND MEDICAL TREATMENT.

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Endocrinol Jpn; 28(2):197-205 1981

A summary of the results of treatment over a period of 18 yr of 27 patients (5 male, 22 female) with Cushing's disease is presented. Adrenalectomy was performed on 21 patients (19 total bilateral adrenalectomy, 2 unilateral adrenalectomy): 4 died of causes not directly related to the operation. Nine bilaterally adrenalectomized patients had hyperpigmentation despite cortisol replacement therapy (20-30 mg/day) and elevated plasma ACTH levels not completely suppressed by daily 2, 4, or 8 mg dexamethasone po or 2.5 mg bromocriptine. Pituitary adenomectomy by the transsphenoidal approach was performed on five patients. Three were cured but one has required postoperative cortisol replacement therapy for hypopituitarism for 1 yr to this date, and two have had a recurrence of Cushing's syndrome after 6-8 mo remissions (1 successfully treated with bromocriptine). Various medical treatments were attempted. Reserpine (1-2 mg/day for 2 yr) and cyproheptadine (24 mg/day) were ineffective and the patients so treated later underwent adrenalectomy; bromocriptine (2.5 mg/day) effectively lowered plasma ACTH, plasma cortisol, and urinary 17-hydroxycorticosteroid in 2/6 patients. The findings are compared with reports in the literature. (20 Refs)

19. EXTRANEURAL METASTASES IN CHILDHOOD BRAIN TUMORS.

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Ann Neurol; 10(3):261-265 1981

Extraneural metastases of primary CNS tumors are extremely rare, having a frequency of perhaps only 0.4-0.5%. Among 36 children with brain tumors treated with a combination of surgery, radiotherapy, and chemotherapy over a period of 12 yr, 5 have had documented evidence of extraneural metastasis (4/15 at autopsy and 1 had extraneural extension diagnosed while alive). The cases of these five patients (3 boys, 2 girls; ages 8, 14, 8, 9, and 10, respectively) are reviewed in an effort to discover a probable cause for this inordinately high incidence of extraneural metastasis. Two had extraneural metastases associated with medulloblastoma and one each with ependymoma, primitive neuroectodermal tumor, and unclassified glioma. All underwent at least one surgical procedure and were aggressively treated with similar courses of radio- and chemotherapy. The prolonged survival of these patients may have permitted growth of sufficient generations of extracranial metastatic cells so that these foci became clinically evident. It is also possible that chemotherapy may alter a patient's immune system in such a way as to promote extracranial tumor growth. (19 Refs)

OTHER THERAPY OF CNS MALIGNANCIES

20. PRIMITIVE NEUROECTODERMAL TUMORS OF CHILDHOOD. AN APPROACH TO THERAPY.

Duffner PK, Cohen ME, Heffner RR, Freeman AI

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J Neurosurg; 55(3):376-381 1981

Primitive neuroectodermal tumors are found in the cerebrum of children and young adults. They are clinically highly malignant and have a rapid course from diagnosis to death. Their microscopic pathology reveals 90% to 95% nondifferentiation, frequent mitoses, and small dark cells with no observable cytoplasm. This paper discusses the treatment of three children with this tumor with a combination of surgery, irradiation, and combination chemotherapy. The results of this approach are compared with previous reports in the literature. The av survival in this series is 24 mo versus approx 8 mo reported in the literature. (Author abstract) (11 Refs)

21. HYPERTHERMIA FOR BRAIN TUMORS: BIOPHYSICAL RATIONALE.

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Neurosurgery; 9(3):327-335 1981

The biophysical basis for the use of hyperthermia in cancer is reviewed, and in particular, the rationale of its application to the problem of malignant brain tumors. Hyperthermia is effective against poorly vascularized and metabolically quiescent tissues, its biological effect is related to the duration and intensity of its application, it appears to have no cumulative toxicity, and it potentiates the effects of both chemotherapy and ionizing radiation at the cellular level. The cellular and antineoplastic effects of hyperthermia are relatively independent of cell cycle and metabolic considerations, and the effects are potentiated by hypoxia and inadequate tissue cooling. The safety and feasibility of both small and large field heating in the human brain has been demonstrated by at least three different techniques. The use of microwaves for hyperthermia of brain tumors is described. The single radiator/sensor is currently being used in Phase I clinical trials in order to establish technical feasibility, patient safety, and patient tolerance. Malignant brain tumors in humans are unable to dissipate heat efficiently, compared to the normal feline brain. The use of multiple interstitial microwave radiator/sensor systems in conjunction with computed tomographic scanners and treatment planning computers may allow complete and effective heating of unresectable human brain tumors. (81 Refs)

OTHER CLINICAL ASPECTS OF CNS CANCER

22. CENTRAL NERVOUS SYSTEM LEUKEMIA AND LYMPHOMA: COMPUTED TOMOGRAPHIC MANIFESTATIONS.

Pagani JJ, Libshitz HI, Wallace S, Hayman LA
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AJNR; 2(5):397-403 1981

Experience with the intracranial computed tomographic (CT) manifestations of leukemic and lymphomatous masses in 405 patients (245 with leukemia, 148 systemic non-Hodgkin's lymphoma, 12 systemic Hodgkin's lymphoma) is reviewed. After contrast enhancement, 31 patients had intracerebral lesions; the CT abnormalities in these patients were correlated with the underlying malignancy, cerebrospinal fluid cytology, and treatment. All CT studies were performed with an EMI 1010 scanner either immediately after 40 g iv iodine or 1 hr after high dose (80 g iodine) contrast infusion. Abnormalities in 24/245 patients with leukemia included leukemic masses (8), hemorrhage (9), abscesse (2) , and 5 other abnormalities including one each acoustic neuroma, astrocytoma, and methotrexate leukoencephalopathy. The only CT abnormality in 160 lymphoma patients was a tumor mass in 7. CT was normal in 374 patients including 148 with meningeal disease diagnosed by cerebrospinal fluid cytologic examination. Malignant masses before treatment appeared isodense or of greater density with varying amounts of edema. Worsening was indicated by increase in the size or number of masses. After radiation therapy and chemotherapy, a central low density region with an enhancing rim developed. The differential diagnosis of the various abnormalities is discussed. (24 Refs)

23. CT OF THE ADVERSE EFFECTS OF THERAPEUTIC RADIATION OF THE CENTRAL NERVOUS SYSTEM.

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Dept. Radiology, London Hosp., Whitechapal, London E1 1BB, England

AJNR; 2(5):453-460 1981

The computed tomographic features of radiation damage to the CNS as a result of radiation therapy were investigated. One child with acute lymphatic leukemia developed somnolence syndrome that was temporary. Permanent complications were more frequent, and included eight patients with histologically proven radionecrosis and one who developed a meningioma in the radiotherapy field, 13 who developed atrophy, three children who developed calcification of the basal ganglia, one necrotizing leukoencephalopathy, three with mineralizing microangiopathy, infarction due to radiation-induced vascular occlusion, abscess formation, and an acute agonal hemorrhage into areas of histologically proven radionecrosis. The most frequent early CT change of radiation damage is low attenuation in the white matter, which might be misinterpreted as due to tumor progression. The importance of appreciating the CT changes in these conditions and recognizing their significance is emphasized. (39 Refs)

24. INTRAOPERATIVE DELINEATION OF LESIONS IN THE SELLAR REGION WITH METRIZAMIDE.

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AJNR; 2(5):461-464 1981

Forty consecutive patients with clinical and radiologic evidence of lesions in the sellar area underwent transsphenoidal injection of metrizamide (Amipaque). The patients were aged 6-82 yr (av, 48 yr) and included 24 males and 16 females. Pituitary adenomas were diagnosed in 33, chordoma in 1, sphenoidal sinus carcinoma in 1, metastases in 2, craniopharyngioma in 1, 'empty' sella in 1, and neurilemm oma in 1. Less than 1 ml of metrizamide, in a concentration of 190 mg I/ml was gently injected under fluoroscopy. In all cases the extent of the lesion was clearly demonstrated. In one patient presumed to have a pituitary tumor, metrizamide demonstrated 'empty' sella. In approx 50% of the cases, extravasation of some contrast medium outside the confines of the tumor occurred. The vascular system in one patient with pituitary apoplexy was outlined. Extravasation into the subarachnoid spaces occurred only from adenomas with suprasellar extension and was more profuse in recurrent tumors or with forced injection. The clivus was outlined in one patient and the carotid sheath was opacified in three. No clinical or endocrinologic abnormality occurred due specifically to metrizamide. The procedure did not interfere with the histopathologic diagnosis of the biopsy material. Intralesional injection of metrizamide was judged a better method for radiologic visualization of pituitary and parapituitary lesions during surgery than intraoperative pneumoencephalography. (3 Refs)

25. DIRECT VISUALIZATION OF INTRACRANIAL TUMOURS IN STEREOTACTIC AND ANGIOGRAPHIC FILMS BY COMPUTER CALCULATION OF LONGITUDINAL CT-SECTIONS: A NEW METHOD FOR STEREOTACTIC LOCALIZATION OF TUMOUR OUTLINES.

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Acta Neurochir (Wien); 58(1/2):27-35 1981

A new method for the direct transformation not only of a target point, but also of the whole tumor outlines from sagittal, coronal, and oblique computer calculated CT-reconstructions to stereotactic x-ray films of any scale is presented. The role of this method in the stereotactic therapy of intracranial tumors and the possibilities which are thus provided are discussed. (Author abstract) (5 Refs)

26. SUPERIOR SULCUS TUMORS: RESULTS OF IRRADIATION OF 36 PATIENTS.

Komaki R, Roh J, Cox JD, Da Conceicao AL
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Cancer; 48(7):1563-1568 1981

Thirty-six patients with superior sulcus tumors were treated primarily with irradiation at the Medical College of Wisconsin Affiliated Hospitals between 1963-1977. Two patients were Stage II (T2N0) and 34 patients were Stage III (22: T3N0 and 12: T1-3N2). Local control correlated positively with the field size for the thoracic irradiation, but not with total dose (between 40 Gy in 4 wk and 64 Gy in 6 1/2 wk). Thirty-one patients (86%) had relief of symptoms for a median of 12 mo after irradiation. Seventeen patients (47%) achieved local control and showed a significantly longer median survival (26.5 mo vs 6.5 mo) and a higher probability of 5-yr survival (45% vs 0) compared with those who did not. Of 19 patients with local failure, distant metastases developed in 9. The most common first and single metastatic site was the brain. Brain metastases developed in seven patients, six of whom had control of the primary tumor. Three of them were alive at 65, 35, and 25 mo after whole-brain irradiation. The 5-yr actuarial survival rate was 23%. There were no major complications. The prognosis was related to local control, but was unrelated to age, histology, symptoms, and signs at presentation, or mediastinal involvement, perhaps the result of the small number of patients studied. The prognosis for patients with superior sulcus tumors is more favorable than other presentations of carcinoma of the lung, but patients are especially at risk for single-organ brain metastases. Primary external radiotherapy is as effective as combined approaches and has a low complication rate; therefore, it is to be preferred for most patients with apical tumors. (Author abstract) (23 Refs)

27. PSYCHOPATHOLOGY OF CORPUS CALLOSUM TUMORS.

Nasrallah HA, McChesney CM
Psychiatry Service, Veterans Admin. Medical Center, Iowa City, IA
Biol Psychiatry; 16(7):663-669 1981

The psychopathological presentations of five patients with corpus callosum tumors were compared with those of eight patients with unilateral frontal or parietal tumors. Significantly more depressive and dementia symptoms (p less than 0.02 and p less than 0.01, respectively) were found in the patients with corpus callosum tumors, but there were no significant differences in schizophrenic symptoms between the two groups. Two of the three patients with corpus callosum tumors located in the genu experienced delusions and hallucinations, suggesting that the location of the lesion on the corpus callosum may be an important factor for the production of certain psychiatric symptoms, whereas depressive and cognitive symptoms may be produced by lesions anywhere on the anterior half of the corpus callosum. (18 Refs)

28. PATHOLOGY OF THE NEURAL CREST.

Pages A
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Ann Pathol; 1(2):109-119 1981

The neural crest develops at the same time as neural tube formation, between the neural tube and the epiblast. It gives rise to various structures, not only at the site of development, but also in other regions, because of the very rapid diffusion of its cells. Locally, these cells form the leptomeninx and sensory ganglia of spinal and cranial nerves; regionally, sympathetic latero- and pre-vertebral ganglia, paraganglia, adrenal medulla and facio-branchial mesenchyme; remotely, melanocytes, Schwann cells, parasympathetic ganglia and the diffuse endocrine system. In spite of experimental studies, it is not known if the development of the latter structure from the neural crest is total or only partial. In fact, it is necessary to distinguish between the diffuse endocrine system of the APUD series and of the lophoneuro-epithelial type. Neural crest pathology shows considerable variation, therefore, in relation to the large number and great variety of its derivate structures. The involvement of the neural crest in the development of some so-called 'mixed' tumors of the CNS, and nephroblastomas is discussed. The authors comment on the hormonal secretions, endocrine or not, of the deviate structures of the neural crest. (52 Refs) (In FRE)

SELECTED PRECLINICAL ASPECTS OF CNS CANCER

29. THE EFFECT OF HUMAN FIBROBLAST INTERFERON (HUIFN-BETA) ON MALIGNANT TUMORS; IN VITRO EXPERIMENTS (MEETING ABSTRACT).

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Dept. Neurosurgery, Dokkyo Univ. Sch. Medicine, Mibu-machi, Tochigi Prefecture 321-02, Japan
Program and Abstracts of the 22nd Workshop on Selected Topics of the Japanese Society of Neuropathology held in Fukuoka, Japan, 9-11 May, 1981. The Japanese Society of Neuropathology, Kyoto 602, Japan, 136 pp., 1981.

Cultured brain tumor tissues obtained at the time of surgery were treated with HuIFN-beta or lymphocytes. A culture of a medulloblastoma obtained from a 6-yr-old boy was treated, beginning in 1 wk, with 0.7 x 10(1) IU or 0.7 x 10(3) IU of HuIFN-beta per ml three times a wk for 2 wk, and the growth rate was compared with that of the controls. The growth of the tissue in the petri dish containing 0.7 x 10(3) IU of HuIFN-beta per ml was inhibited 86%, as measured by colony area, as compared with the control, which agreed with the clinical effect on this patient. Morphological changes were seen in the cells given 7 x 10(3) IU of HuIFN-beta per ml; the cells generally became long and thin and some had a differentiated astrocyte-like appearance with long projections. The growth of the glioma cell line was not inhibited by the addition of 0.7 x 10(3) IU of HuIFN-beta per ml. The growth of malignant astrocytoma tissue from a 29-yr-old male patient was inhibited by 12%, 65%, and 85% compared to the control when the autochthonous peripheral lymphocytes alone, HuIFN-beta (3 x 10(3) IU/ml) alone, and lymphotes + HuIFN-beta, respectively, were added. The 51Cr release assay using K562 cells as the target cells showed cytotoxicity of 4.7% for HuIFN-beta alone and 40% for the HuIFM-beta + lymphocytes. Cytotoxicity was about 30% when the lymphocytes were incubated with HuIFN-beta for 2 hr, washed and then applied to the target cells. These results indicate that HuIFN-beta has a direct effect on the tumor and an effect mediated by lymphocytes, the greatest tumor growth inhibition or cytocidal effect being produced when HuIFN-beta and the lymphocytes were added together. (no Refs) (In JPN)

30. BIOLOGY OF GLIOMAS: POTENTIAL CLINICAL IMPLICATIONS OF GLIOMA CELLULAR HETEROGEN EITY.

Bigner DD
Dept. Pathology, Duke Univ. Medical Center, Post Office Box 3156, Durham, NC, 27710
Neurosurgery; 9(3):320-326 1981

The morphological, cell biological, biochemical, and immunological heterogeneity of human glioma cells was explored in 11 permanent cell lines derived from anaplastic glioma, glioblastoma multiforme, gliosarcoma, and mixed anaplastic glioma. Four morphological groups were observed: fibroblastic in five cell lines, fascicular in three, epithelial in one (gliosarcoma), and glial in two. Each line, however, was sufficiently distinct morphologically to be recognized as individual. Each line was also distinct with respect to differentiation features, such as percentage of cells responding morphologically to cyclic AMP; 2'3'-cyclic nucleotide 3'-phosphohydrolase enzyme levels, glial fibrillary acidic protein expression, fibronectin levels; monoclonal antibody 81C6 binding ratios; and the expression of normal human brain-specific surface antigens. Four of the lines developed serially transplantable tumors after injection of tumor cells into athymic mice; in two others, the tumors grew initially, then regressed. It is hypothesized that the major determinant of therapeutic resistance is the genotypic and phenotypic heterogeneity of glioma cells. Evidence supporting this hypothesis is reviewed. (40 Refs)

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NEUROGLIAL CELL TUMORS

1. PRIMARY DEMYELINATING DISEASE SIMULATING GLIOMA OF THE CORPUS CALLOSUM. REPORT OF THREE CASES.

Rieth KG, Di Chiro G, Cromwell LD, McKeever PE, Kornblith PL, Kufta CV, Pleet AB
Diagnostic Radiology Dept., NIH, Clinical Center, Building 10, Room 6S211, Bethesda, MD, 20205
J Neurosurg; 55(4):620-624 1981

Computerized tomography (CT) has made it easier to distinguish tumoral from nontumoral diseases of the CNS. In the presence of mass effect, however, this distinction may be difficult or im possible to make. Primary demyelinating disease may occasionally present as a focal cerebral mass. The authors report three cases of primary demyelinating disease of the brain involving the corpus callosum and periventricular white matter and associated with mass effect, which proved difficult to differentiate from infiltrating 'butterfly' gliomas. (Author abstract) (14 Refs)

NEURONAL CELL AND PRIMITIVE BIPOTENTIAL PRECURSOR CELL TUMORS

2. NEURAL TUMORS OF THE NASAL FOSSAE.

Claux J, Vincent P
Service O.R.L., C.H.U. Rangueil, 31054 Toulouse Cedex, France
J Fr Otorhinolaryngol; 30(7):433-436 1981

The development and diagnosis of 15 neural tumors of the nasal fossae are discussed. Some patients benefit from a combination of surgery and radiotherapy and have a good prognosis, and others with neural tumors accompanied by systemic malignant or sarcomatous hematologic disorders, show a less favorable prognosis. These tumors can be derived from three types of olfactory neuroblasts: superficial supportive cells, olfactory cells, and Schwann cells. The diagnosis of these tumors is easy when both supportive and olfactory cells can be identified. Diagnosis is more difficult when only olfactory neurocytes or embryonic tissues are involved. Rosette formation, immunofluorescent studies, and electron microscopy are considered as diagnostic technics. Clinical symptoms important for histological diagnosis include tumor site, presence of associated infection, adenopathy, isolated epistaxis, or nasal obstruction or infection, radioclinical extension, loss of the sense of smell, and signs of intracranial compression. The histological diagnosis of olfactory neuroepitheliomas, neurocytomas, and neuroblastomas is described. The differential diagnosis of these neural tumors and undifferentiated carcinomas, malignant lymphomas, and sarcomas is described. (34 Refs) (In FRE)

3. CLINICAL EVALUATION OF SEQUENTIALLY SCHEDULED CISPLATIN AND VM26 IN NEUROBLASTOMA: RESPONSE AND TOXICITY.

Hayes FA, Green AA, Casper J, Cornet J, Evans WE
St. Jude Children's Res. Hosp., Memphis, TN, 38101
Cancer; 48(8):1715-1718 1981

Cis-dichlorodiammineplatinum (CDDP) and VM26, both of which have been proven efficient in treating neuroblastoma, were combined in a sequential schedule and administered to 22 children with disseminated neuroblastomas resistant to treatment with cyclophosphamide and doxorubicin (adriamycin). During this same study, 14 children were prospectively evaluated for the effect of the CCDP on magnesium metabolism and the effect of induced hypomagnesemia on parathyroid function. Complete or partial tumor responses were achieved in 6 and 9 cases, respectively and were of prolonged duration (longer than 6 mo) in 8 of the 15 responding. It was also shown that CDDP-induced hypomagnesemia is the result of excessive renal loss and is severe enough to interfere with the normal parathormone response to hypocalcemia. (Author abstract) (16 Refs)

4. SHUNT THERAPY IN MEDULLOBLASTOMA? (MEETING ABSTRACT).

Voth D, Schwartz M, Huwel N
Neurosurgical University Clinic, Mainz, W. Germany
Acta Neurochir; 56(3/4):278 1981

The danger of dissemination of tumor cells in medulloblastoma by ventriculoatrial or ventriculo-peritoneal drainage for the treatment of hydrocephalus internus occlusus should induce a certain caution. In order to avoid a hematogenous tumor cell implantation or an implantation into the peritoneum we have recently performed ventriculocisternotomy as an internal drainage. The technical complications of this intervention are minimal. After the posterior craniotomy with total or subtotal resection of the tumor, and after visualization of the sometimes dilated mesencephalic aqueduct, a lamellar catheter, is pushed through the aqueduct and the 3rd ventricle so far that its end is placed in one of the two anterior horns. Subsequently, the distal part of the catheter is inserted into the spinal cerebrospinal fluid space. We followed-up 21 patients with such a Leksell drainage. Beside the indication described by Leksell, we see today another indication in subtotally resected or in malignant tumors of the posterior cranial fossa in which a recurrence can be expected. An indication can also be seen in benign lesions (pilocytic astrocytoma) if these extend to the aqueduct outlet and if a postoperative stenosis of the aqueduct due to swelling or reactive gliosis seems possible. The functional safety of the Leksell drainage has the same size factor as the Torkildsen drainage. (no Refs)

5. EFFECTS OF INTRALESIONAL INTERFERON ON NEUROBLASTOMA: CHANGES IN HISTOLOGY AND DNA CONTENT DISTRIBUTION OF TUMOR MASSES.

Sawada T, Takamatsu T, Tanaka T, Mino M, Fujita K, Kusunoki T, Arizono N, Fukuda M, Kishida T
Dept. Pediatrics, Kyoto Prefectural Univ. Medicine, Kamikyoku, Kyoto 602, Japan
Cancer; 48(10):2143-2146 1981

Local injections of interferon, 30 x 10(4) IU, 10x, were found to reduce masses of neuroblastoma. Histologic findings and nuclear DNA measurements of cells from tumors in which interferon has been injected compared with cells from tumors that did not receive injections demonstrated that the reduction of neuroblastoma masses by interferon did not depend on increased cell differentiation or on interruption of tumor cell production. Although the mechanism of interferon's action on reducing neuroblastoma is unknown, the disappearance of tumor cells may be caused by high levels of interferon in tumor tissues. (Author abstract) (8 Refs)

TUMORS OF THE CRANIAL AND SPINAL NERVE ROOTS

6. PROGNOSIS AND THERAPY OF METASTATIC TUMORS OF THE SPINE.

Rinker D
No affiliation given
Adv Neurosurg; (9):490-493 1981

A review of 77 cases treated for metastatic malignant spinal tumors during the period 1959-1980 was made. Mean patient age was 46.4 yr; of 58 males and 19 females, known malignant disease was present in 48 cases. In 23 additional cases the primary tumor could be detected. Primary tumor distribution included 44 metastases of carcinoma, 12 metastases of solid sarcoma, 4 malignant melanomas, 6 plasmacytomas, 3 Hodgkin's disease and lymphoid sarcoma, and 8 tumors of rare type (pleuromesothelioma, neuroblastoma, malignant pheochromocytoma, Wilms' tumor of the kidney, and 4 unidentified). On admission greater than 3/5 patients were paraparetic, half of them paraplegic. Treatment consisted predominantly of laminectomy and consecutive radiotherapy (52 cases). Clinical results were: neurological improvement in 13 cases, no change in 52, and deterioration in 12. Previously incurable back and radicular pain was palliated in 51 cases. Six patients died within 1 mo of admission; mean survival time was approx 1.95 yr. In 37 cases with tumors of worst prognosis (bronchial, anaplastic, and hypernephroid carcinoma and malignant melanoma), death occurred less than 6 mo following treatment. Results were discouraging, despite the alleviation of pain in most patients. Operation will no longer be performed on paraparetic patients with only minor functions intact, and in cases of known bronchial carcinoma or apoplectic paraparesis. (13 Refs)

7. POSTERIOR FOSSA APPROACH FOR REMOVAL OF ACOUSTIC NEURINOMAS. RECENT EXPERIENCE.

Harner SG, Laws ER
Mayo Clinic, Rochester, MN, 55905
Arch Otolaryngol; 107(10):590-593 1981

Herein we review our experience with surgical removal of acoustic neurinomas in 74 patients from January 1978 through December 1980. The surgical approach was through the posterior fossa. Total removal was accomplished in 73 of 74 patients, and there were no surgical or postoperative deaths. The facial nerve was preserved in 54 patients, and hearing was preserved in 5 (21% of patients with small tumors). We believe that this approach to acoustic neurinomas has the advantages of being universally applicable, having a low complication rate, and possessing the potential of saving both facial and cochlear function. (Author abstract) (9 Refs)

TUMORS OF THE LYMPHORETICULAR SYSTEM AND BLOOD VESSELS

8. MALIGNANT LYMPHOMA OF NERVE TISSUE: STUDIES ON CASES DIFFICULT TO DIAGNOSE (MEETING ABSTRACT).

Maya K, Llena JF, Hirano A
Dept. Neuropathology, Montefiore Hosp., Medical Center, Bronx, NY, 10467
Program and Abstracts of the 22nd Annual Meeting of Japanese Society of Neurology held in Kumamoto, Japan, 20-22 May, 1981. Japanese Society of Neurology, Tokyo 113, Japan, 282 pp., 1981.

Eight cases of malignant lymphoma could be diagnosed only by histological examin ation of biopsy and autopsy specimens during the past 5 yr. Malignant lymphoma could be diagnosed by biopsy in three patients, two of whom showed tumor formation with local and progressive symptoms similar to other space-occupying lesions. The presurgical diagnosis for these patients was glioblastoma multiform. The other patient had partial paralysis for 2 yr, and the tumor cells did not form a tumor but had infiltrated into the subarachnoid space and perivascular cavity of the cortex. Diagnosis could not be made before death in five patients who were 60 to 70 yr old and who had acute or subacute onset and rapid advance. The symptoms and findings of these patients varied or worsened step by step during the course of the illness, mental symptoms also occurring frequently. Clinical diagnosis was bilateral cerebrovascular disorder for one patient, and Creutzfeldt-Jacob's disease was suspected for two. The fifth patient was suspected of having Creutzfeldt-Jacob's diseases from the clinical course but was later suspected of having a brain tumor after neural radiographic tests. The pathologic findings in all of these patients were diffuse invasion of the tumor cells into the pia matter, subarachnoid space, perivascular cavity and parenchymal nerve tissue, being similar to the development of viarl meningoencephalitis. Tumor formation, hemorrhage or infarction may also be seen in the lesion, which obscures the clinical view. Therefore, when various nervous symptoms are present, and the onset, course or findings are abnormal in elderly patients, malignant lymphoma should be suspected and diagnosis made by nerve radiography and by histologic examination of brain biopsy specimens. (no Refs) (In JPN)

TUMORS OF THE CHOROID PLEXUS AND PINEAL REGIONS

9. PINEAL REGION TUMORS: COMPUTED TOMOGRAPHIC-PATHOLOGIC SPECTRUM.

Futrell NN, Osborn AG, Cheson BD
(c/o Osborn) Dept. Radiology, Univ. Utah Coll. Medicine, 50 North Medical Dr., Salt Lake City, UT, 84132
AJR; 137(5):951-956 1981

While several computed tomographic (CT) studies of posterior third ventricular neoplasms have included descriptions of pineal tumors, few reports have concentrated on these uncommon lesions. Some authors have asserted that the CT appearance of many pineal tumors is virtually pathognomonic. A series of nine biopsy-proved pineal gland and eight other presumed tumors is presented that illustrates their remarkable heterogeneity in both histopathologic and CT appearance. These tumors included germinomas, teratocarcinomas, hamartomas, and other varieties. They had variable margination, attenuation, calcification, and suprasellar extension. Germinomas have the best response to radiation therapy. Biopsy of pineal region tumors is now feasible and is recommended for treatment planning. (Author abstract) (21 Refs)

SECONDARY TUMORS OF THE CNS

10. GAS CISTERNOGRAPHY ('MINIGAS') FOR PREOPERATIVE AND PEROPERATIVE EVALUATION OF PITUITARY ADENOMAS (MEETING ABSTRACT).

Eldevik OP
Neuroradiological Department, Ulleval Hospital, Oslo, Norway
Acta Neurochir; 56(1/2):120 1981

From October 1978 to May 1980 45 patients with pituitary tumors have been operated on transnasally at our hospital. The preoperative neuroradiological work-up of these patients consisted of skull films, computed tomography, gas cisternography and angiography, in this order. Preoperative gas cisternography was done on a polytomography table with fluoroscopy. A lateral C1-C2 puncture with gauge 22 spinal needle was performed under fluoroscopic control. Then 5 to 15 ml oxygen was insufflated, filling the prepontine and suprasellar cisterns. Lateral and frontal tomograms of the sella, sphenoidal sinus, and posterior nasal cavity were obtained. A good visualization of the suprasellar cistern with possible suprasellar growth of the pituitary tumor was obtained as well as thin-section tomograms of the sella and sphenoidal sinus. Preoperative gas cisternography was performed by the neuroradiologist in the operating room with lateral fluoroscopy of the sellar region during the operation. A lateral C1-C2 puncture was performed, and the needle was left in place during the operation for refill of gas. We used 3-5ml gas at a time, up to a total of 30 ml. During the neurosurgical evacuation of the pituitary tumor the neuroradiologist was present in the operating room using fluoroscopy of the gas-filled cisterns to guide the neurosurgeon and reduce the risk of this critical part of the operation. (no Refs)

11. ACTH-PRODUCING ADENOMAS IN CUSHING'S DISEASE (MEETING ABSTRACT).

Muller OA, Fahlbusch R, Stass P, Scriba PC
Neurochirurgische Klinik, University of Munich, Munchen, W. Germany
Horm Res; 13(4/5):341 1981

In the last 8 yr we observed 30 patients with ACTH-dependent Cushing's disease (CD), who were operated upon the pituitary, and 16 patients with Nelson's syndrome (NS). (a) In 28 patients with normal or slightly enlarged sella, transsphenoidal exploration of the pituitary was performed. Up to now, 19 patients showed clinical and hormonal remission without necessity of long-term hormonal replacement therapy. In the majority of these cases a transitory adrenal insufficiency was documented. Preoperative ACTH levels are helpful for the prognosis of operative therapy of pituitary ACTH excess. (b) In 2 patients with larger invasively growing adenomas a radical hypophysectomy and irradiation were performed. One patient died because of tumor invasion into the hypothalamus, the other patient is in remission since 3 yr. In 11 of 16 patients with hyperpigmentation, sella enlargement and high ACTH levels after bilateral adrenalectomy, a pituitary operation became necessary. In contrast to the high normalization rate in patien ts with CD, ACTH levels were normalized in only 3 of the 11 patients with NS, in whom radical hypophysectomy and combined cryo- and radiotherapy were performed. In the majority of cases with CD, a primary pituitary defect has to be assumed. Therefore sella exploration is the method of choice as the first therapeutical step. It can be assumed, that this therapeutical management of patients with CD may prevent NS in the future. (no Refs)

12. IMMUNOCYTOCHEMICAL CLASSIFICATION OF PITUITARY ADENOMAS (MEETING ABSTRACT).

Attramadal A, Nesbakken R, Torjesen PA
Institute of Pathology, Rikshospitalet, Oslo, Norway
Acta Neurochir; 56(1/2):122 1981

Studies of pituitary adenomas have clearly shown that classification of these tumors, based on granule staining properties, into acidophil, basophil, and chromophobe has outlived its usefulness. Functional classification based on the hormones secreted seems to be more informative. We have used an immunocytochemical method for identification of the hormones produced by by the adenoma cells. The specificity and sensitivity of this technique appear appropriate for accurate assessment of the functional status of pituitary adenomas and for functional classification. Biopsy specimens from human pituitary adenomas were examined for the hormones produced by the immunoperoxidase (PAP) technique using high titre antisera. In order to assess the validity of functional classification based on this method, the results were correlated with corresponding levels of circulating hormones measured preoperatively by radioimmunoassay. Forty-two human pituitary adenomas were examined. Twenty of the tumors showed only or mainly prolactin producing cells whereas 12 were exclusively or predominantly composed of cells containing growth hormone. One tumor possessed exclusively cells with thyroid stimulating hormone. Four of the tumors displayed about equal amounts of growth hormone and prolactin producing cells, while twelve more tumors showed scattered cells with hormone production different from that of the main type. Prolactin and growth hormone were the hormones mostly involved. In six of the tumors no hormone producing cells were detectable. The immunocytochemical results correlated excellently with the levels of circulating hormones measured preoperatively. (no Refs)

13. REMISSION OF CUSHING'S SYNDROME WITH HYPERSECRETION OF ACTH AND PROLACTIN DURING BROMOCRIPTINE THERAPY (MEETING ABSTRACT).

Winkelmann W, Allolio B, Heesen D, Hipp FX, Mies R
Innere Medizin II der Universitat Koln, Koln, W. Germany
Acta Endocrinol [Suppl]; 96(240):62 1981

In patients with pituitary tumors, hypersecretion of 2 or 3 pituitary hormones has occasionally been observed. The combination of hypersecretion of ACTH with growth hormone (GH) and/or prolactin (PRL) is extremely rare. In patients with Cushing's syndrome (CS) a test dose of bromocriptine (Br) is followed by a drop in plasma ACTH, whereas long-term application has no effect. Long-term suppression of ACTH by Br was also lacking in a patient with hypersecretion of ACTH, GH, and PRL. The following case report concerns a 46-yr-old male patient with CS due to a pituitary tumor with hypersecretion of ACTH and PRL. By x-ray tomography a microadenoma was recognized at the bottom of the sella turcica. Cortisol (F) and pituitary hormones were measured by radioimmunoassay. Both urinary and plasma F were found to be elevated. Plasma ACTH also was elevated. Dexamethasone failed to suppress plasma F which increased during ACTH or lysine-vasopressin administration. A test dose of Br led to a strong decrease of PRL, ACTH, and F. We therefore started a continuous therapy with Br going on until now for about 8 mo. Plasma PRL, as well as ACTH and F were already normalized 10 wk after starting the therapy. The max doses of 15 mg Br could be reduced to 7.5 mg/day very soon. Normalization of adrenal regulation was demonstrated by an effective dexamethasone suppression of plasma F and a sufficient F increase during insulin-induced hypoglycemia. At no time was hormonal replacement therapy necessary. Within 4-6 mo a clinically complete remission of CS was obvious. Since hypersecretion of ACTH and PRL was stopped by a dopamine agonist a disturbance of dopaminergic neurotransmission seems to be involved in the pathogenesis of this case. Although the combined hypersecretion of ACTH and PRL in CS is extremely rare, the effect of Br observed in our patient should suggest measurement of PRL in all cases of central CS. (2 Refs)

14. IMPARIED PITUITARY RESPONSE TO BROMOCRIPTINE SUPPRESSION: REVERSAL AFTER BROMOCRIPTINE PLUS TAMOXIFEN (MEETING ABSTRACT).

Volker W, Gehring WG, Zur Muhlen AV
Medizinische Hochschule Hannover, Hannover, W. Germany
Acta Endocrinol [Suppl]; 96(240):71 1981

The present study was undertaken on the assumption that bromocriptine plus tamoxifen might have a synergetic effect in previously resistant cases of prolactinoma to bromocriptine monotherapy. Twelve women aged 16 to 54 were tested. Two of them were unable to take bromocriptine because of severe side-effects, the others were under longterm bromocriptine therapy. Nine women had sellar or supraseliar enlargement, five of them having undergone incomplete surgical resection. The others had normal sella tomograms, but suppression was poor or impossible. Ten women continued taking bromocriptine, but additionally received tamoxifen 10 mg bid. Blood samples were taken before the beginning of combined therapy and one of four wk later. Prolactin (PRL), luteinizing hormone, follicle-stimulating hormone, estradiol and progesterone were determined by radioimmunoassay. The two women who had previously been unable to take bromocrip tine were able to accept it in conjunction with tamoxifen. The combination with tamoxifen resulted in a marked suppression of PRL in six out of ten patients. In four cases there was no effect at all. In the three women with normal sella, PRL was suppressed to normal values. In the cases with sellar or suprasellar tumors the addition was successful in three, unsuccessful in four. No correlation was found between this effect and the extent of the tumor. In both women who tolerated bromocriptine when tamoxifen was added, PRL was suppressible. One woman conceived shortly after the combined therapy had been started. In six women spontaneous bleedings occurred, only in four of them had PRL been suppressed sufficiently. Basal body temperature curves became normal in three women, galactorrhea ceased in five. One woman reported a marked improvement of libido. The suppressive effect of bromocriptine on PRL secretion is enhanced by addition of tamoxifen in most cases of adenomatous hyperprolactinemia. Side-effects of bromocriptine are considerably improved by tamoxifen. (6 Refs)

OTHER THERAPY OF CNS MALIGNANCIES

15. COMPUTERIZED TOMOGRAPHY (CT) AND DOSE OPTIMIZATION IN THE IRRADIATION OF BRAIN TUMORS (MEETING ABSTRACT).

Marks JE
Mallinckrodt Institute of Radiology, St. Louis, MO
The Symposium on Computed Tomography in Radiotherapy, September 18-19, 1981, Arlington, Virginia American Association of Physicists in Medicine; :F2 1981

Since 1974 the author has routinely used CT scans to plan optimum dose distributions in the irradiation of brain tumors. Dose optimization, or concentration of radiation in the tumor with relative sparing of surrounding brain, requires a CT scan to demonstrate the spatial relationship between tumor and surrounding brain, a high energy x-ray beam, 10 MeV or greater, and the ability to reconstruct the dose distribution onto the CT image. To establish a rationale for dose optimization the author reviews the known dose response information for glioblastoma multiforme and cerebral radionecrosis within the range of radiation doses most commonly used. Theoretically, dose optimization maximizes the effects of radiation on the tumor and reduces the chance of radiation injury to the surrounding brain. Practically, it is used to spare hair and reduce the incidence of radiation damage to cranial soft tissues. (no Refs)

OTHER CLINICAL ASPECTS OF CNS CANCER

16. PRELIMINARY RESULTS OF INTRACAVITARY IRRADIATION OF CYSTIC CRANIOPHARYNGIOMAS BY MEANS OF STEREOTACTICALLY APPLIED YTTRIUM-90.

Sturm V, Rommel T, Strauss L, Georgi P, Scheer KE, Steude U, Stock G, Penzholz H, Backlund EO
No affiliation given
Adv Neurosurg; (9):401-404 1981

Treatment of 10 cystic patients with craniopharyngiomas by intracavity high energy beta-irradiation of the cyst wall is described. Following stereotactic puncture of the center of the cyst, 1-2 ml of craniopharyngioma fluid was aspirated and replaced by Technetium-99 soln to determine the exact vol of the cyst. The amount of colloidal yttrium-90 necessary to irradiate every point of the inner surface of the cyst with 20,000 rad was injected into the cyst. The yttrium-90 instillation caused an arrest in the growth of 8/9 cysts in one group of patients. In the single patient in the second group, another small cyst developed from the tumor matrix 10 mo after treatment of the first cyst. (11 Refs)

17. CT-AIDED STEREOTAXY FOR FUNCTIONAL NEUROSURGERY AND DEEP BRAIN IMPLANTS (MEETING ABSTRACT).

Mundinger F, Birg W
Department of Stereotaxy and Neuronuclearmedicine, Neurosurgical University Clinic, Freiburg, W. Germany
Acta Neurochir; 56(3/4):245 1981

Computed tomography (CT) has improved and augmented stereotactic indications. This applies to functional neurosurgery, which makes it possible to reach larger nuclear and neuronal structures without ventriculography and to perform lesioning, or to implant electrode systems. CT advantages also apply to non-functional neurosurgery, where the target points can be localized exactly by incorporating computed tomography into the stereotactic localization procedure. CT information can also be employed for Curie Therapy by interstitial implantation using iodine-125 seeds in non-resectable tumors and for the implantation of catheter systems in cases of hydrocephalic enlargement of ventricles, tumor, or arachnoid cysts. This information is incorporated into the dosimetry and localization procedures, the position of the implant can be observed, and the morphological effect can be controlled. It is necessary to reconstruct the level of the CT layers. For this purpose we have developed a cylindrical, radiolucent hood with markings. This is fixed to the base ring of the computer-stereotaxy device developed by Riechert and Mundinger and modified by Mundinger and Birg, but it can also be attached to the frame of other stereotactic devices. The CT layers are transferred with the base ring and the hood. The layers are arranged using a program which can be put into a pocket calculator. If it is possible to achieve an identical positioning of the 0-point of the stereotactic device in the CT scanner, the hood can be eliminated. We have produced additional holders for the base ring. The stereotaxy-computer system that we have developed can be put into the CT computer as a complete package. (no Refs)

SELECTED PRECLINICAL ASPECTS OF CNS CANCER

18. EFFECT OF BROMOCRIPTINE, SOMATOSTATIN, AND OESTRADIOL-17BETA ON HORMONE SECRETION AND ULTRASTRUCTURE OF HUMAN PITUITARY TUMOURS IN VITRO.

Prysor-Jones RA, Kennedy SJ, O'Sullivan JP, Jenkins JS

Dept. Medicine, St. George's Hosp. Medical Sch., London, SW17 ORE, England

Acta Endocrinol (Copenh); 98(1):14-23 1981

The effect of bromocriptine and somatostatin on hormone secretion and the ultrastructure of human pituitary adenomas was studied in vitro. Prolactin secretion was inhibited by bromocriptine in 3 out of 10 prolactin-secreting tumors and in explants from two normal pituitaries. GH secretion was reduced by bromocriptine in four out of six GH-secreting adenomas but was not affected by the drug in the incubations of normal pituitaries. Somatostatin inhibited GH secretion in two out of five pituitary adenomas and the effect was comparable with that of bromocriptine. Incubation of prolactin-secreting adenomas with estradiol for a long as 24 days produced no change in hormone secretion. Examination of tumor explants by electron microscopy showed that somatostatin and bromocriptine produced accumulation of secretion granules but no changes in the secretory organelles. Long term bromocriptine treatment of 'nude' athymic mice bearing xenografts of human pituitary adenomas suppressed hormone secretion and produced some increase in secretion granules but there were no morphological changes in the secretory organelles or other vital structures of the adenoma cells. (Author abstract) (27 Refs)

19. PHARMACOLOGY AND TOXICITY OF INTRACAROTID ADRIAMYCIN ADMINISTRATION FOLLOWING OSMOTIC BLOOD-BRAIN BARRIER MODIFICATION.

Neuwelt EA, Pagel M, Barnett P, Glassberg M, Frenkel EP

Div. Neurosurgery, Univ. Oregon Health Science Center, 3181 South West Sam Jackson Park Road, Portland, OR, 97201

Cancer Res; 41(11,part1):4466-4470 1981

The effect of reversible blood-brain barrier modification on the delivery of Adriamycin to the brain was studied in a rodent and canine model. Pharmacokinetic and physiological studies were done in these animals after a wide range of doses of Adriamycin (0.1 to 1.0 mg/kg) were administered into the carotid artery following osmotic barrier modification with mannitol. In the absence of barrier modification, no immunoreactive Adriamycin was detected in the cerebrum; whereas, following barrier modification, up to 4.5 ug of drug and/or metabolites per g of brain were found. Optimum tissue levels of Adriamycin and metabolites were achieved following barrier modification when the drug was administered by either bolus or slow continuous (15-min) infusion. Immunoreactive drug was identified in brain for up to 6 hr after administration. Significant functional neurotoxicity occurred at all dose levels, even at 0.1 mg/kg, a level at which Adriamycin concentration in the brain was below the level of detectability. Neuropathological examination revealed the presence of necrosis and hemorrhagic infarcts. Thus, these pharmacological and toxicity studies suggest that Adriamycin (or its metabolites) may produce significant clinical neurotoxicity when even small amounts penetrate the blood-brain barrier. (Author abstract) (23 Refs)

20. XENOGRAFT OF HUMAN MALIGNANT GLIAL TUMORS INTO BRAINS OF NUDE MICE. A HISTOPATHOLOGICAL STUDY.

Horten BC, Basler GA, Shapiro WR

(c/o Shapiro), Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021

J Neuropathol Exp Neurol; 40(5):493-511 1981

Sixteen of 21 human malignant glial tumors were successfully heterotransplanted into the brains of nude mice, and one other was transplanted into the brain after prior sc heterotransplantation. Most xenografts grew preferentially as diffusely infiltrating tumors within hemispheric white matter, generally sparing cortex and deep gray matter. The heterogeneity of most in vivo human tumors gave way to a tumor of generally uniform cell type while growing in nude mice. From six human tumors, all glioblastomas, there emerged histologic patterns or cell forms that were not evident in the original tumor. Tumors from 15 patients were treated with standard chemotherapeutic agents while growing in nude mouse brains. The most common morphologic change induced in tumors by several agents was a distinctive giant cell change characterized by large bizarre nuclei and abundant cytoplasm. It is concluded that the human brain-tumor-nude-mouse xenograft model offers morphological parallels with the clinical situation, but selects for growth only some of the many subpopulations of the human tumor. Such selection imposes restrictions on the clinical inferences that may be drawn from this model. (Author abstract) (17 Refs)

21. GROWTH CHARACTERISTICS OF HUMAN GLIOMA-DERIVED AND FETAL NEURAL CELLS IN CULTURE.

Icard C, Liepkalns VA, Yates AJ, Singh NP, Stephens RE, Hart RW (c/o Yates) Dept. Pathology, Neuropathology Unit, Ohio State Univ., 473 West 12th Ave., Columbus, Ohio, 43210

J Neuropathol Exp Neurol; 40(5):512-525 1981

Growth characteristics of human fetal neural cells (CH) and human glioblastoma multiforme-derived cells (12-18) in culture were compared. Cells were grown to confluent densities of 38,000 to 42,500 cells/cm2 for CH and 85,800 to 87,100 for 12-18. Population doubling times were 40.0 +-5.1 hr and 66.5 +-9.8 hr for CH and 12-18 cells, respectively. The mean DNA content per cell of the glioma-derived cells was twice that of the fetal brain cells at sparse, log, and confluent cell densities. High concentrations (40%) of serum in growth medium increased DNA contents in confluent CH, but not 12-18, cells. The amount of protein per cell also was consistently higher in glioma cells than CH cells, but, as cell densities increased, protein contents decreased for both: 1200 to 700 pg/cell in glioma cells, and 840 to 560 pg/cell in CH cells. In each cell line, initial rates of [3H]ThdR incorporation into TCA precipitable material decreased as cell density increased, but confluent glioma-derived cells incorporated 10x more [3H]ThdR than confluent fetal cells. Almost all CH cells had a normal diploid chromosome number of 46. A histogram showing the relative frequencies of chromosome numbers of glioma-derived cells had peaks of 52, 79, and 105 chromosomes per metaphase, indicating a haploid number of 26 for most cells. Lengths of cell cycle phases, determined using autoradiographic techniques, indicate that glioma-derived cells had a longer generation time and S period than fetal neural cells. These data demonstrate several biological differences between glioblastoma-derived cells and non-neoplastic fetal neural cells, indicating that this system is of potential value for comparative studies on growth control and contact inhibition. (Author abstract) (31 Refs)

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CNS MALIGNANCIES

Diagnosis, Treatment

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NEUROGLIAL CELL TUMORS

1. TREATMENT OF MALIGNANT GLIOMAS WITH VINDESINE (MEETING ABSTRACT).

Alavi JB, Bruno LA, Weller CB
University of Pennsylvania, Philadelphia, PA
Twelfth International Congress of Chemotherapy, July 19-24, 1981, Florence, Italy. The International Society of Chemotherapy 301 pp., 1981.

Nine patients (age 29-62 yr) have been treated with Vindesine as second chemotherapy for glioblastoma multiforme, Grade III or IV. These patients had progressive disease documented b y computed tomographic (CT) scan, and required corticosteroids for control of intracranial pressure or relief of neurologic symptoms. All had previously received whole brain radiation (7 to 33 mo before Vindesine) and nitrosourea chemotherapy (for 3 to 17 mo before Vindesine). Five of 9 patients were not ambulatory. Treatment was Vindesine 2 mg/m2 x one wk, 2.5 mg/m2 x one wk, then 3 mg/m2 weekly. Toxicity consisted of mild sensory neuropathy. loss of deep tendon reflexes and 4 patients with transient leukopenia (WBC 2600-3100/mm(3)), one patient with thrombocytopenia (92,000/mm(3)). After six wk of treatment three patients were symptomatically improved, and two of these had better computed tomographic scans. Overall, five patients progressed at 4,6,8,10 and 16 wk; two patients are stable at 18 and 22 wk; two patients have had significant (greater than 30%) improvement of tumor size by CT scan, persisting for 16 and 32 wk. The corticosteroid dose is stable or decreased in all stable and responding patients, and the longest survivor has had resolution of papilledema and no longer requires steroids. Glioblastoma is a highly malignant tumor, and responses to second agents are rare. We conclude that Vindesine has activity in this disease with minimal toxicity. (no Refs)

2. LARGE DOSE FRACTION IRRADIATION AND METRONIDAZOLE IN THE TREATMENT OF GRADE IV GLIOBLASTOMA MULTIFORME (MEETING ABSTRACT).

Kapp DS, Wagner FC
Department of Therapeutic Radiology, Yale University School of Medicine, New Haven, CT, 06510
Conference on Chemical Modification: Radiation and Cytotoxic Drugs, September 17-20, 1981, Key Biscayne, Florida. Committee for Radiation Oncology Studies 139 pp., 1981.

The survival of patients with Grade IV glioblastoma multiforme of the cerebral hemispheres remains extremely poor with local failure occurring in 95% or more of the patients. Radiation survival curves obtained on cultured human glioblastoma cell lines have exhibited large shoulders - possibly reflecting the capacity of these cells to repair sublethal damage. Recent clinical trials have demonstrated improved survival in patients with Grade IV glioblastoma multiforme treated with the hypoxic cell sensitizer metronidazole in conjunction with suboptimal radiation therapy treatment schedules, compared to irradiation alone. In an attempt to overcome the possible radioresistance of glioblastoma multiforme related to the large shoulder on the in vitro survival curves and to sensitize hypoxic tumor cells, a treatment protocol was instituted utilizing large dose fraction irradiation therapy in conjunction with the hypoxic cell sensitizer metronidazole. Patients with biopsy-confirmed, previously untreated cerebral Grade IV glioblastoma multiforme were, following surgery, irradiated once a wk at 600 rads per fraction, four hr after ingestion of metronidazole, 6 g/M2. A total of seven treatments were employed. Five treatments were given to the whole brain using parallel opposed lateral portals; the final two treatments were given using planned fields encompassing the entire gross tumor vol as determined by computerized transaxial tomographic (CAT) scan. All patients were maintained on antiseizure medications and corticosteroids. Serial metronidazole levels were determined prior to each treatment and patients were followed closely clinically. and with serial CAT scans. Eighteen patients have been entered on this study. The treatment was, in general, well tolerated. The majority of patients experienced varying degrees of gastrointestinal upset lasting up to several hr following metronidazole administration. One bed-confined patient died of pulmonary emboli. One patient experienced moderately severe ototoxicity. (1 Ref)

3. REOPERATION FOR GLIOBLASTOMA.

Young B, Oldfield EH, Markesbery WR, Haack D, Tibbs PA, McCombs P, Chin HW, Maruyama Y, Meacham WF
Univ. Kentucky Medical Center, MS107, 800 Rose St., Lexington, KY, 40536
J Neurosurg; 55(6):917-921 1981

The results of a second operation for tumor removal in 24 adult patients with supratentorial glioblastoma multiforme or anaplastic astrocytoma were analyzed. The median survival time after reoperation was 14 wk. Five of the 24 patients lived 6 mo or longer after reoperation. Only three of these patients maintained a Karnofsky rating (KR) of at least 60 for 6 mo or longer after reoperation. Preoperative neurological status (KR) is the most significant determinant of survival after reoperation ($p = 0.02$). When the KR is at least 60, median survival after reoperation is 22 wk. When the KR prior to reoperation is less than 60, median survival is 9 wk. Only 1 of 13 patients with a KR of less than 60 prior to reoperation survived longer than 6 mo after the second operation. The interval between first and second operation is significantly related to survival ($p = 0.03$), but when adjustment is made for the KR the interoperative interval is no longer significantly related to survival after the second operation ($p = 0.39$). Age, sex, and location of tumor were not significantly related to duration of survival. This study suggests that reoperation is most likely to produce the best result when the KR is at least 60 and the interval between operations is longer than 6 mo. Using these criteria, one-third of the patients could be expected to survive with a KR of at least 60 for 6 mo. The study indicates that reoperation should not be carried out when the KR is less than 60. (Author abstract) (13 Refs)

NEURONAL CELL AND PRIMITIVE BIPOTENTIAL PRECURSOR CELL TUMORS

4. EXTRANEURAL METASTATIC MEDULLOBLASTOMA DURING CHILDHOOD.

McComb JG, Davis RL, Isaacs H, Hoffman HJ, Quest DO
1300 North Vermont Ave., Suite 903, Los Angeles, CA, 90027
Neurosurgery; 9(5):548-551 1981

Factors that possibly correlate with extraneural metastasis (ENM) were studied in 59 children with histologically verified medulloblastoma (MB). Of these patients, 49/59 died and 34/49 were autopsied. Of the 34 autopsied patients in whom MB had arisen in the cerebellar vermis, 6 had ENM. Two of these six patients presented with neck masses before any surgical procedure. In autopsied patients with ENM, the mean age at initial diagnosis was 3.25 yr compared with 5 yr for patients without

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metastasis. A 3:2 male:female sex ratio ratio was reported (35:24 for the entire group and 21:13 for those autopsied). Five of six ENM patients were male. The role of surgical tumor seeding in ENM is discussed. Radiation and chemotherapy did not seem to play any role in the incidence of ENM. In the six children with ENM, the metastatic tumors were located in the neck in two cases, the ribs in three, a vertebra in one, the liver in three, and the lung in two. All six ENM patients had diffuse involvement of the entire subarachnoid space. None of the ENM patients had a desmoplastic MB; this MB type was present 6/28 of the patients without ENM. The length of survival after initial diagnosis of MB was 0-11 mo (mean 4 mo). In those patients without ENM, survival was slightly greater than 1 yr. (24 Refs)

5. THERAPY FOR NEUROBLASTOMA AT STAGE III AND IV (MEETING ABSTRACT).

Uchino J, Sasaki F, Shinada K, Ikeda T, Naito H, Une R, Hata Y, Kasai Y
First Dept. of Surgery, Hokkaido Univ., Sch. Medicine, Sapporo-shi, Hokkaido, 060, Japan
Nippon Shonigeka Gakkai Zasshi; 17(3):431 1981

Of the 20 patients who had neuroblastoma at Stage III or IV and had received large dose therapy of cyclophosphamide (CPA), 15 had the CPA therapy before surgery. Almost all of the tumor could be extirpated in nine of these patients, most of the tumor could be extirpated in four and only partial resection could be performed on two. Surgery could be performed again after a certain period on four patients, and the paraaortic lymph nodes could be dissected almost completely in one of these patients. Four recent patients were given 0.1 mg of vincristine (VCR) per kg to induce synchronization 24 hr before the CPA large dose therapy. Two patients on whom complete lymph node dissection was performed by second operation were both still alive with no signs of recurrence 3 mo and 15 mo after the second operation. In patients who did not have lymph node dissection performed, relapse occurred in one patient who was still alive 18 mo and the others died at 10 mo. CPA therapy before and after surgery made it possible to extirpate almost completely about 60% of the primary lesions that were otherwise difficult to resect, and to completely dissect the regional lymph nodes by a second-look operation after a certain period, thus almost totally preventing local relapse and worsening. The prognosis for the patients who have rapid advance and systemic metastasis 8 mo after surgery or later is expected to be improved by CPA large-dose therapy following synchronization by VCR during the complete remission stage after surgery, and by combined therapy with adriamycin, 5-(3,3-dimethyl-1-triazeno)-1H-imidazole-4-carboxamide and cisplatinum. (no Refs) (In JPN)

MESODERMAL TUMORS OF THE CNS

6. MALIGNANT MENINGIOMA: CLINICAL AND PATHOLOGICAL FEATURES.

Thomas HG, Dolman CL, Berry K
(c/o Dolman) Pathology Lab., Vancouver General Hosp., 855 West 12th Ave., Vancouver, British Columbia V5Z 1M9, Canada
J Neurosurg; 55(6):929-934 1981

The records of 15 patients with a diagnosis of malignant meningioma were reviewed. In one of these patients, in whom invasion of the brain and pituitary gland was the only unusual feature, the tumor was reclassified as benign. Seven tumors, four hemangiopericytomas and two transitional and one syncytial meningioma, were considered to be only borderline-malignant despite necrosis and invasion of the brain, because of few mitoses and regular architecture. Of this group of patients, four men and three women, two are alive and well, three died after incomplete resections, and two succumbed to recurrent tumor that had become inoperable. The other seven patients, six men and one woman, had lesions classified as histologically frankly malignant, on the basis of marked anaplasia and numerous mitoses. These comprised three hemangiopericytomas and three syncytial and one fibrous meningioma. One of these patients is alive and well and the others are dead, three as a result of metastases. The initial clinical course of malignant meningiomas tends to be short but is otherwise indistinguishable from that of benign meningiomas. The chances of recurrence and eventual death are high, and extracranial metastases are not rare. The tumors are most often hemangiopericytomas, but not exclusively so, and men are particularly at risk. (Author abstract) (36 Refs)

7. ARTERIAL EMBOLIZATION OF MENINGIOMA: TECHNICAL CONSIDERATIONS.

Mitomo M, Kawai R, Miura T, Nishikubo Y, Harada K, Ikeda T, Mogami H
Dept. Radiology, Osaka Univ. Sch. Medicine, Osaka, Japan
Neurol Surg; 9(3):295-304 1981

Five cases (4 women, 1 man; 30-60 yr old) of meningioma which were embolized prior to surgical resection were reported. The meningiomas were located in the right parietal convexity, left parasagittal area, right middle fossa, posterior fossa, and frontal convexity. Spongostan special, a gelatin sponge material, was injected via the external carotid artery in two sizes (1 x 1 x 1 mm and 1 x 1 x 40 mm) to occlude intratumoral and terminal peripheral branches and parent arteries, respectively. When terminal branches of the parent meningeal artery supplied the meningioma, small emboli were injected first to occlude the terminal peripheral tumor vessels, then large emboli were injected to occlude the parent meningeal artery and prevent reflux of the smaller emboli. When the tumor was supplied by meningeal branches of the parent artery, the parent artery was occluded with a large emboli just behind the tumor vessels, then tumor vessels were embolized with smaller emboli and a final large emboli, conserving distal portions of the parent superficial artery via collateral circulation. Surgical resection of the meningiomas were performed successfully in all five cases with reductions in bleeding and operation time due to the embolizations in all five cases. (7 Refs) (In JPN)

8. PHASE II TRIAL OF HUMAN FIBROBLASTIC INTERFERON IN MALIGNANT GAMMAPATHIES AND MENINGEAL LEUKEMIA (MEETING ABSTRACT).

Misset JL, Gastiaburu J, Goutner A, De Vassal F, Mathe G
ICIG, Inserm U-50, Hospital Paul-Brousse, 94800-Villejuif, France
Twelfth International Congress of Chemotherapy, July 19-24, 1981, Florence, Italy. The International Society of Chemotherapy 301 pp., 1981.

Eighteen patients (16 myelomas and 2 Waldenstrom's disease) were submitted to a phase II trial of human fibroblastic interferon (RPMI) given iv: 6 million units weekly (Group A: 7 patients) or 3 million units twice weekly (group B: 11 patients). Three patients stopped treatment after 3.3 and 15 infusions for major side effects. Other side-effects were minor and more pronounced in group A. Reduction in M component greater than 50% of initial value was not seen. More than 25 percent was seen in 3 patients. Response became significant only after 3 mo in one patient. Bence Jones proteinuria disappeared in one patient. Bone marrow plasmocytosis decreased greater than 50% in 4 patients and bone pain was significantly decreased in 5 patients. Natural killer (NK) activity studies in these patients did not show clear correlation between level of activity prior or after treatment and response. Patients having meningeal relapse of acute lymphoid leukemia (4 patients) and leukemic lymphosarcoma (1 patient) were given interferon: 1.3 million units daily or qod up to remission or failure. Four patients failed to improve after 5 to 8 injections (and given methotrexate) 1 complete remission was obtained after 11 injections and is still maintained under chemotherapy. Tolerance was good in all cases. NK activity studies were not performed in this five patients. Further studies are warranted in these two clinical situations. (no Refs)

TUMORS OF THE CRANIAL AND SPINAL NERVE ROOTS

9. POSSIBLE CELLULAR IMMUNITY AGAINST ACOUSTIC NEUROMA.

Rasmussen N, Thomsen J, Tos M
Univ. ENT Dept., Rigshospitalet, Blegdamsvej 9, DK-2100 Copenhagen, Denmark
Acta Otolaryngol (Stockh); 92(3/4):337-341 1981

Leukocyte migration capillary tube technique (LMCT) was used on WBC from 11 patients prior to acoustic neuroma surgery and 16 healthy control persons. The LMCT was carried out against acoustic neuroma extract, produced prior to the study, the with use of normal temporal lobe extract as control antigen. Four patients and one control person exhibited consistent cell-mediated immunity (CMI) against acoustic neuromas. The method is of no diagnostic value, but the results are sufficiently spectacular to merit further research. (Author abstract) (9 Refs)

10. NEUROEPITHELIOMA--A RARE MALIGNANT PERIPHERAL NERVE TUMOR OF PRIMITIVE ORIGIN: REPORT OF TWO NEW CASES AND A REVIEW OF THE LITERATURE.

Harper PG, Pringle J, Souhami RL
(c/o Souhami) Dept. Radiotherapy and Oncology, Univ. Coll. Hosp., Gower St., London WC1, England
Cancer; 48(10):2282-2287 1981

Two cases of primitive neuroectodermal primary peripheral nerve tumors (neuroepitheliomas) are presented. They both demonstrated the rosette pattern described by Homer Wright indicating their neuroectodermal origin, and were unlike Schwann cell tumors. In one case, intensive chemotherapy with local radiotherapy had resulted in a disease-free interval of 30 mo at the time of this report. These cases support the existence of neuroepithelioma as a distinct tumor type. (Author abstract) (20 Refs)

TUMORS OF THE LYMPHORETICULAR SYSTEM AND BLOOD VESSELS

11. INVESTIGATION OF COMPUTED TOMOGRAPHY FOR CEREBELLAR HEMANGIOBLASTOMA.

Nakao S, Kikuchi H, Matsumoto A, Karasawa J, Arimitsu T
Dept. Neurosurgery, Natl. Cardiovascular Center, Japan
Neurol Surg; 9(3):277-283 1981

Preoperative plain and enhanced computed tomographic (CT) findings of six cases of cerebellar hemangioblastoma (5 men, 1 woman; av 50.6 yr old) were studied. An Electronic Music Industries (EMI)-1010 scanner was used with 100 ml of 65% Angiographin. Profiles of x-ray absorption values were made in 5/6 cases. Two types of hemangioblastomas were distinguishable with CT, a solid type that is an isodensity mass surrounded by a low density rim, and a cystic type that is shaped like a cyst and has mural nodules in the cyst wall. In 2/3 cases of solid type hemangioblastomas an irregularly shaped cyst was observed with enhanced CT in the central portion of the tumor. Enhanced CT patterns of the mural nodules in the cystic type tumors showed variation in x-ray absorption values, but the mural nodules in the solid type tumors showed consistent x-ray absorption values. Although CT was thought to be reliable for demonstrating solid tumors, cystic components, and tumor-associated hydrocephalus, vertebral angiography was thought to be an important adjunct to show the vascular nature of the tumor and mural nodules, so both should be us ed for preoperative diagnosis of hemangioblastomas. (8 Refs) (In JPN)

12. PRIMARY BRAIN LYMPHOMAS. ANATOMOCLINICAL, ULTRASTRUCTURAL AND IMMUNOCYTOCHEMICAL STUDY ABOUT 23 CASES.

Hassoun J, Andrac L, Gambarelli D, Toga M
Laboratoire d'Anatomic Pathologique et de Neuropathologie, 27, Boulevard Jean Moulin, F 13385 Marseille Cedex 5, France
Ann Pathol; 1(3):193-203 1981

Twenty-three cases of primary brain lymphomas were morphologically studied. Electron microscopy was done in 12 cases and immunoperoxidase reactions for light chains of Ig in 10 cases. The patients were 14 males and 9 females. Except two children, the mean age was 50 yr. Clinical features and pre-operative investigations lacked any specificity. Post-operative radiotherapy could be performed in 13 patients, 11 of them being still alive with a follow-up varying from 2.5 mo to 4.5 yr. All the other patients pursued fulminating course (max: 4.5 mo). Tumors were preferentially located in frontal and temporal lobes. On gross examination, well limited tumors were more frequent than ill-defined or purely infiltrating tumors. Microscopically, all the lymphomas were of the diffuse type. Perivascular clusters of lymphoma cells, meningeal and parenchymal infiltrates and sub-ependymal sprouts were found in the peritumoral areas. The lymphomas were cytologically characterized according to the modified Kiel classification using light and electron microscopic data. Thirteen lymphoblastic lymphomas (with 1 convoluted-cell type), 1 centroblastic lymphoma, 8 immunoblastic lymphomas (2 with plasmacytic differentiation) were identified. Light chains of human Ig were immunocytologically demonstrated in 6 of 12 tumors tested, all the positive cases corresponding to immunoblastic lymphomas. A unique case of primary meningeal Hodgkin's disease was found. These results were compared with the rare previous reports associating these different morphological investigations. (Author abstract) (26 Refs) (In FRE)

TUMORS OF THE CHOROID PLEXUS AND PINEAL REGIONS

13. PINEAL TUMORS IN CHILDREN AND ADOLESCENTS. TREATMENT BY CSF SHUNTING AND RADIOTHERAPY.

Abay EO, Laws ER, Grado GL, Bruckman JE, Forbes GS, Gomez MR, Scott M
(c/o Laws) Dept. Neurologic Surgery, Mayo Medical Sch., Mayo Clinic, Rochester, MN, 55905
J Neurosurg; 55(6):889-895 1981

Tumors of the pineal region account for 3% to 8% of pediatric intracranial tumors. The treatment of such tumors has been in a state of flux between conservative therapy (cerebrospinal fluid shunting and radiotherapy) and direct surgical removal. A brief history and review of the literature with analysis of both approaches is given, and the Mayo Clinic's experience with conservative treatment of tumors in the pineal region in patients 20 yr and younger (27 cases) is studied and analyzed. The series comprises 21 boys and 6 girls, with an age range of 1 to 20 yr (mean 13.7 yr). Follow-up examinations are complete and range from 1 to 24 yr, with a mean follow-up period of 7.8 yr. The median survival time for these patients treated with shunt and radiotherapy is 17.7 yr. There was no mortality from treatment and complications were rare. The details of the clinical presentation, diagnostic findings, pathology, therapy, recurrence, and survival are presented. All patients under 6 yr of age (6 cases) had recurrences, 50% in other areas in the brain and 50% in the spinal cord, perhaps pointing to the need for whole-brain and spinal-axis irradiation in patients in this age group. The results of this study of the conservative approach form a standard against which results of any other type of therapy may be compared. (Author abstract) (53 Refs)

SECONDARY TUMORS OF THE CNS

14. HYPERPROLACTINEMIA IN MAN: CLINICAL INDICATIONS AND THERAPY.

Eversmann T, Eichinger R, Fahlbusch R, Rjosk HK, Von Werder K (c/o von Werder), Medizinische Klinik Innenstadt, Ziemssenstrasse 1, D-800 Munchen 2, W. Germany
Schweiz Med Wochenschr; 111(47):1782-1789 1981

Fifty-seven male patients with hyperprolactinemia have been investigated. Macroadenomas were found in 49 patients of whom 24 had received pituitary surgery before elevated PRL levels were discovered. In eight patients radiology of the pituitary fossa revealed either evidence of microadenoma or a completely normal sella turcica. Prolactin levels ranged from 582 to 498,000 uU/ml. All patients with macroprolactinomas, including those who had undergone previous surgery, had PRL levels above 5,000 uU/ml. Disturbances of libido and sexual potency were prevalent in the majority of patients, less frequently accompanied by gynecomastia and galactorrhea. However, visual disturbances were the reason for the first visit to the doctor in the majority of patients. Pituitary surgery led to improvement of visual field defects, though prolactin levels were never normalized. Postoperative radiotherapy had no significant influence on PRL levels. In contrast, bromocriptine therapy led, in the majority of patients not only to improvement of hypogonadal symptoms but also to normalization of PRL levels. (Author abstract) (28 Refs) (In GER)

15. BENSERAZIDE, A STIMULATOR OF PROLACTIN RELEASE: A NEW TEST IN THE DIAGNOSIS OF PITUITARY PROLACTIN-SECRETING TUMOURS.

Pontiroli AE, Falsetti L, Voltolini AM, Alberetto M, Pellicciotta G, De Pasqua A, Girardi AM, Pozza G
Ospedale San Raffaele, 20132 Milano, Italy
Acta Endocrinol (Copenh); 98(3):326-332 1981

Benserazide, an extra-cerebral inhibitor of dopa-decarboxylase, elicits prolactin (Prl) release in normal subjects when administered po. The aims of this study were to characterize the effect of benserazide on Prl release and to evaluate benserazide as a diagnostic tool in hyperprolactinemic patients. In normal subjects, the effect of 50 mg benserazide is reduced to a greater extent by 500 mg than by 200 mg l-dopa, and is nullified by dopamine (DA, 50 mg iv in 180 min), which also decreases fasting plasma Prl levels. Doses of 25, 50 and 150 mg benserazide elicit Prl responses which are slightly and progressively but not significantly higher; a second dose of 50 mg, administered 150 min later, is without effect on Prl release, while TRH (200 ug iv) elicits a further Prl peak. Since it is known that consecutive doses of TRH yield progressively lower Prl responses while 5-hydroxytryptophan (the precursor of serotonin) further increases Prl release in response to benserazide, we hypothesize that, in an area involving both the hypothalamus and the pituitary gland, anti-DA drugs (benserazide), TRH, and serotonin stimulate Prl release by interacting with different kinds of receptors. When administered to hyperprolactinemic patients, benserazide stimulated Prl release in puerperal women and in patients with functional hyperprolactinemias, but was totally ineffective in patients with pituitary adenomas, whatever the fasting plasma Prl levels. on two patients with a normal sellar tomography in whom benserazide induced no Prl release, a second tomography or computerized axial tomography of the brain, performed respectively 3 and 6 mo later, revealed a pituitary microadenoma. These results suggest that benserazide may be a valuable diagnostic tool in the differential diagnosis of hyperprolactinemia. (Author abstract) (19 Refs)

16. PATTERNS OF CORTICOTROPIC CELLS IN THE ADULT HUMAN PITUITARY IN CUSHING'S DISEASE.

McNicol AM
Univ. Dept Pathology, Royal Infirmary, Glasgow, Scotland
Diagn Histopathol; 4(4):335-341 1981

Pituitary glands from nine patients who died of Cushing's disease were studied. Staining with an immunoperoxidase technique revealed three patterns of corticotropic cells. Three pituitaries showed a pattern which could not be distinguished from normal. Three pituitaries contained an ACTH cell adenoma and a marked reduction in the total number of ACTH cells in the remainder of the gland; two of the tumors were microadenomas, but the whole tumor of the third adenoma was not available for assessment. In the third group, two of the pituitaries contained large aggregates of ACTH cells which by size and morphological appearance had been diagnosed as adenomas; the third pituitary showed hyperplasia of ACTH cells with nodules but without a large aggregate of ACTH cells. Two populations of corticotrophic cells may exist within the adult human pituitary; the populations appear to correspond to the anatomical distribution of anterior and intermediate lobe corticotrophs. (46 Refs)

17. PITUITARY CUSHING'S SYNDROME AND NELSON'S SYNDROME: DIAGNOSTIC CRITERIA, SURGICAL THERAPY, AND RESULTS.

Guthrie FW, Ciric I, Hayashida S, Kerr WD, Murphy ED
(c/o Ciric), 2500 Ridge Ave., Evanston, IL, 60201
Surg Neurol; 16(5):316-323 1981

Eight patients with pituitary Cushing's syndrome and two with Nelson's syndrome were followed from 1 to 10 yr after removal of pituitary adenomas. A detailed assessment of the pituitary-adrenal axis was obtained in all patients when last seen save the first, who had undergone a complete hypophysectomy 10 yr previously. Long-term observations have shown sustained endocrine cure in seven of eight patients with pituitary Cushing's syndrome. One patient with Nelson's syndrome was also cured. There was no operative morbidity or mortality. There were no instances of diabetes insipidus. The long-term results in this study indicate that patients with pituitary Cushing's syndrome have a better than 90% chance of being cured after transsphenoidal removal of the pituitary (micro) adenomas. Current diagnostic and therapeutic concepts in the management of pituitary Cushing's syndrome are discussed in detail. (Author abstract) (97 Refs)

OTHER THERAPY OF CNS MALIGNANCIES

18. PRELIMINARY REPORT ON ANTITUMORIGENIC ACTIVITY OF CIS-DICHLORODIAMINE PLATINUM IN METASTATIC BRAIN TUMORS.

Kolaric K, Roth A, Jelicic I, Matkovic A
Dept. Chemotherapy and Neurosurgery, Central Inst. Tumors and Allied Diseases, Ilica 197, 41000 Zabreb, Yugoslavia
Tumori; 67(5):483-486 1981

In spite of pharmacokinetic studies, which have shown that only cis-DDP traces are found in brain tissue, cytotoxic activity of this drug in primary brain tumors has recently been reported. The purpose of our study was to examine whether cis-DDP also has antitumor properties in metastatic brain tumors. Twelve consecutive untreated patients with brain metastases recorded by CAT scans or radionuclide scans plus neurologic examinations underwent the treatment. Histology of primaries revealed four bronchial, three breast, one gastric, one colorectal carcinoma, two melanomas, and one soft tissue sarcoma. Cis-DDP was administered at the doses of 30 mg/m2 body surface daily for 4 days. All the patients were evaluated. Objective response (3 complete and 2 partial remissions) was observed in 5 of 12 patients (response rate 42%). Three stable disease cases were also noted; however, in the remaining four patients the disease in the brain progressed. Complete response (5 mo) was observed in a breast cancer patient, in a melanoma (4+ mo), and in a microcellular bronchial cancer (2+ mo). Two partial responses (lung, breast) lasted 2+ and 2+ mo. Toxicity was moderate but tolerable for the patients. The preliminary results of this study show that cis-DDP possess antitumorigenic properties also in patients with metastatic brain tumors, which has not been proved till now. (Author abstract) (15 Refs)

19. INTERNAL IRRADIATION FOR CYSTIC CRANIOPHARYNGIOMA.

Kobayashi T, Kageyama N, Ohara K
Dept. Neurosurgery, Nagoya Univ. Sch. Medicine, 65, Tsuruma-cho, Showa-ku, Nagoya, Japan
J Neurosurg; 55(6):896-903 1981

The authors report the results of internal irradiation with labeled chromic phosphate (32P) and gold-198 (198Au) colloid in eight cases of cystic craniopharyngiomas. They used a newly developed dosimetric formula, by which the radiation dose at the cyst wall and at any point far from the radioactive source can be calculated. Ten courses of irradiation in eight patients were carried out by injection of either 32P or 198Au colloid into the cyst through an Ommaya drainage system that had been placed at craniotomy. Follow-up studies ranging from 13 to 156 mo revealed that all cysts were effectively treated, with elimination of fluid or collapse of the cyst. This was confirmed by Conray cystography and/or computerized tomography. Not only the dose delivered to the wall but also the thickness of the cyst wall and the location of the cyst are important factors in planning internal irradiation. A safe and adequate dose to the cyst wall could range between 9,000 to 30,000 rads for craniopharyngioma. This treatment is suitable for large cysts that are thought to be difficult to remove radically, recurrent cysts resistant to previous treatment, or multiple cysts. Internal irradiation may also be applicable in other cystic intracranial tumors if dosimetry is calculated accurately. (Author abstract) (19 Refs)

20. PERMANENT AND REMOVABLE IMPLANTS FOR THE BRACHYTHERAPY OF BRAIN TUMORS.

Gutin PH, Phillips TL, Hosobuchi Y, Wara WM, Mackay AR, Weaver KA, Lamb S, Hurst S
(c/o Editorial Office), Dept. Neurological Surgery, 350 Parnassus Ave., Suite 807, San Francisco, CA, 94117
Int J Radiat Oncol Biol Phys; 7(10):1371-1381 1981

Brachytherapy was employed in 37 patients with primary or metastatic brain tumors. Forty implantations with 192Ir, 198Au or 125I by stereotactic neurosurgical techniques were used. Most tumors had recurred after surgery, whole brain irradiation, and chemotherapy. Sixteen implants were permanent while 24 were in plastic catheters inserted through burr holes. One or more sources were positioned in each tumor to deliver 3,500-7,350 rad to the tumor periphery for 198Au, 4,000-12,000 rad for 192Ir, and 3,000-20,000 rad for 125I. In six patients treated with 192Ir, three had objective responses for 2, 4 and 12 mo; two were stabilized for 8 and 11 mo. Among 11 treated with 198Au, three of seven evaluable patients responded for 3, 5 and 37+ mo. A patient who received an interstitial booster dose with 198Au after whole brain irradiation stabilized for 15 mo before development of spinal metastases. Among six who received permanent implants of low activity 125I, three with glioblastomas or anaplastic astrocytomas continued to deteriorate, presumably because dose rate was too low. One patient with a low-grade astrocytoma (optic chiasm) responded dramatically to permanent, low activity 125I; another, with hypothalamic glioma, responded and was stable for 9 mo when external radiation was used. Seventeen removable high activity 125I sources were implanted in 15 patients with recurrent malignant primary or metastatic tumors. Of 12 presently evaluable, eight patients responded for 4-8 mo, three stabilized for 3, 7, and 11 mo, while one patient with a metastatic melanoma failed to improve despite two implants, 8 wk apart. (17 Refs)

OTHER CLINICAL ASPECTS OF CNS CANCER

21. MYELOGRAPHY WITH AMIPAQUE IN INFANTS AND CHILDREN.

Schmidt RC, Vogelsang H

Abteilung fur Neuroradiologie, Medizinische Hochschule Hannover, Karl-Wiechert-Allee 9, D-3000 Hannover 61, W. Germany

Radiologe; 21(11):521-526 1981

Results of myelography with the water-soluble contrast medium Amipaque (Metrizamide: AP) in 47 children are presented. Chief indication for the procedure was suspicion of intraspinal tumor or malformation of spinal cord. AP (2.5-10 ml, concentration 170 mg I/ml) was injected with fluoroscopic control. Doses were determined individually in each case. Pathologic myelograms were obtained in 27 cases. Condition detected included meningomyelocele, lipoma, dermatoid tumor, and teratoma. Dysrhaphic disturbances in the cervical and thoracic regions in two cases were traced to spinal cord atrophy. Four extradural and two intramedullary tumors unrelated to malformations were detected. Myelograms using AP were marked by better visualization of fine detail than that obtained with gaseous or oily contrast media. AP allowed demonstration of the spinal cord, subarachnoidal space, nerve roots, and normal and pathological vasculature. Side effects were minimal in children, in contrast to previous results with adults. (37 Refs) (In GER)

22. RECENT ADVANCES IN NEURO-OTOLOGY.

Brackmann DE

2122 W. Third St., Los Angeles, CA, 90057

Head Neck Surg; 4(1):22-28 1981

Auditory brain-stem response audiometry, electroneuronography, the cochlear implant, and the infratemporal fossa approach to the skull base are described. An extended infratemporal approach which permits resection of large temporal bone tumors and lesions situated in the clivus and parasellar or parasphenoid region is illustrated with two case histories. A 47-yr-old woman had a glomus tumor removed 16 yr before presentation; since that time she had had total loss of hearing in the right ear. Investigation of a pulsatile mass revealed a vascular tumor filling the right external auditory canal; removal of a recurrent glomus tumor from the neck was unsuccessful. The technique for removal of tumors of the clivus, parasellar, and parasphenoid regions is outlined. Polytomography in a 50-yr-old woman with a partially removed posterior fossa meningioma showed extensive involvement of the petrous apex. Extended infratemporal fossa approach exposed the entire recurrent tumor involving petrous apex, cavernous sinus, and cranial nerves 9, 10, and 11. Details of the operative technique are presented. Postoperative course was uneventful. Three mo postoperatively, no return of extraocular movements or facial function had occurred. However, performance 6 mo postoperatively of anastomosis between ansa hypoglossi and facial nerve may lead to recovery of function. (14 Refs)

23. FINE NEEDLE ASPIRATION BIOPSY OF DEEP CEREBRUM: A COMPARISON BETWEEN NORMAL AND NEOPLASTIC MORPHOLOGY (MEETING ABSTRACT).

Crain BJ, Bigner SH, Johnston WW

Department of Pathology, Duke University Medical Center, Durham, NC

Twenty-ninth Annual Scientific Meeting of the American Society of Cytology, November 2-7, 1981, St. Louis, Missouri. The Society 90 pp., 1981.

Proper interpretation of thin needle aspiration biopsies of deep-seated cerebral lesions requires familiarity with normal morphologic structures as well as with neoplastic and non-neoplastic conditions which involve this region. We therefore compare 22-gauge needle aspirates of deep white matter, basal ganglia, and thalamus from autopsies of three neurologically normal adult males with eight aspirates from tumors which occur in this location. Smears and Millipore filter preparations of needle washings were fixed in 95% ethanol and stained by the Papanicolaou method. Normal white matter contained oligodendrogila with small, dark, round nuclei and astrocytes with larger, bland, oval nuclei and occasional cytoplasmic extensions. In comparison, nuclei of astrocytomas were more variable in size and shape with prominent elongated cytoplasmic processes producing a markedly fibrillar background. Glioblastoma multiforme was more cellular with irregular or clefted nuclei, inconspicuous necleoli, and sparse cytoplasmic processes. Basal ganglia and thalamus consisted largely of neurons with large nuclei and prominent nuceoli. Although individual neurons were alarming, sparse cellularity distinguished these normal tissues from malignant gliomas and metastatic tumors. Knowledge of the normal morphology of deep cerebral structures by fine needle aspiration is necessary to avoid erroneous diagnoses of neoplasia. (no Refs)

SELECTED PRECLINICAL ASPECTS OF CNS CANCER

24. PHARMACOKINETICS OF A NEW WATER-SOLUBLE NITROSOUREA, 1-(2-CHLOROETHYL)-3-(METHYL-ALPHA-D-GLUCOPYRANOSE-6-YL) 1-NITROSOUREA (MCNU) IN BRAIN TUMORS.

Harada K, Kiya K, Kobayashi M, Takeda T, Mukada K, Uozumi T

Dept. Neurosurgery, Hiroshima Univ., Sch. Medicine, Kasumi, Hiroshima 734, Japan

Gan To Kagaku Ryoho; 8(5):735-742 1981

We investigated the pharmacokinetics of a newly developed water-soluble nitrosourea derivative, MCNU (1-(2-Chloroethyl)-3-(methyl-alpha-D-glucopyranose-6 yl)-1-nitrosourea) in three cases of malignant glioma and three cases of metastatic brain tumor following one-shot iv injection. A major portion of the MCNU was excreted in the urine. The pharmacokinetics was estimated by two-compartment open model analysis. The distribution rate was very fast, the half-life of alpha-phase being 4.4 min. The elimination rate was slow, the half-life of beta-phase being 41 min, and 65.4% of the MCNU moved into the tissue compartment. The MCNU level in the cerebrospinal fluid (ventricle) in two cases of metastatic brain tumor was measured. The max concentration of MCNU was 0.37 ug/ml 40 min after iv injection and corresponded to 30.5% of the level in the blood. the max MCNU level in malignant glioma tissue was 2.38 ug/g at 10 min and 3.31 ug/g in metastatic brain tumor tissue at 20 min. MCNU tended to move into glioma and metastatic brain tumor tissue. These results suggest that MCNU moves into brain tumor tissue and cerebrospinal fluid and that it may become a candidate drug for brain tumors. (26 Refs) (In JPN)

25. MULTICELLULAR TUMOUR SPHEROIDS FROM HUMAN BRAIN TUMORS. A MODEL FOR EXPERIMENTAL CHEMOTHERAPY IN VITRO? (MEETING ABSTRACT).

Oktar N, Darling JL, Thomas DG
Department of Neurological Surgery, Institute of Neurology, Queen Square, London WC1N 3BG, England
Cell Biol Int Rep; 5(SupplA):42 1981

Multicellular tumor spheroids have been obtained from a range of fourteen primary and secondary human brain tumors. Tumor biopsies were minced, disaggregated with collagenase and the resultant cell suspension diluted to 5x10(5) cell/ml and inoculated into flasks coated with 0.5% agar. After approx one wk in static culture, single spheroids (mean vol 1.4 x 10(6) um(3)) were transferred into individual agar coated wells on a microtitration plate. At least 10 spheroids were used for each trial. They were exposed to graded concentrations of various chemotherapeutic agents (lomustine, Procarbazine, Vincristine, VM-26, Adriamycin, Mithramycin, L-asparaginase and Methotrexate) for 24 hr at 37 C. After treatment, drugs were removed, the spheroids washed and refed with fresh growth medium. The growth medium of treated and non-treated (control) spheroids was changed twice weekly throughout the assay. The spheroids were measured daily using an eye piece um for a 10 day period following drug removal and the growth delay calculated. Spheroids were also disaggregated after drug treatment and the colony forming efficiency in soft agar was determined. A dose dependant correlation was observed between both relative growth delay and cell survival with these cytotoxic agents. However, patterns of chemotherapeutic response were found to vary considerably between different tumor types and even between tumors of similar histopathology. The effects of corticosteroids, interferon and cyclic nucleotides on human tumor multicellular spheroids was also assessed using the same system. Spheroids produced from human brain tumors may be useful as models for the study of general biology as well as a model for experimental in vitro chemosensitivity. (no Refs)

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CNS MALIGNANCIES

Diagnosis, Treatment

SERIES CT18 No. 82/05

MAY, 1982

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NEUROGLIAL CELL TUMORS

1. A STUDY OF DEXAMETHASONE RECEPTOR PROTEIN IN HUMAN GLIOMAS.

Rengachary SS, Tilzer LL
Dept. Surgery, Kansas Univ. Coll. Health Sciences and Hosp., Kansas City, KS, 66103

J Surg Res; 31(6):447-455 1981

Glucocorticoids provide symptomatic relief when administered to patients with malignant brain neoplasms. Though improvement in peritumoral brain edema is thought to be the primary effect, a direct growth inhibitory effect of steroids cannot be ruled out. Available experimental data pertaining to the growth inhibitory effect of steroids are inconclusive. In this study we have attempted to reexamine this question by assay-

HE 20. 3173/2:

ing the glucocorticoid receptor protein in the human glial neoplasms. Subject to certain constraints described in the study, glucocorticoid receptor protein is not detectable in the glial tumors. A critical analysis of the composite evidence obtained from clinical observations, and experimental studies suggest that glucocorticoids administered in the usual pharmacological doses have no direct growth inhibitory effect on human glial tumors. (Author abstract) (58 Refs)

2. RADIATION EFFECTS ON MALIGNANT GLIOMAS AND ON THE SURROUNDING BRAIN (MEETING ABSTRACT).

Schiffer D, Giordana MT, Soffietti R, Sciolla R

II Neurological Clinic, University of Turin, Turin, Italy

UICC Conference on Clinical Oncology, October 28-31, 1981, Lausanne, Switzerland. International Union Against Cancer 131 pp., 1981.

Forty-five operated and not operated malignant gliomas have been irradiated and treated by chemotherapy. The whole brain has been cut into coronal sections and histologically studied. In the tumor immediate and late effects have been identified. They are represented by central necroses, decrease of mitoses, macrophages, vessel wall degeneration, etc and are more pronounced after super-fractionated radiation. In the surrounding brain a delayed radionecrosis was observed in 15% of cases, with typical clinicotomographic and pathologic characteristics. Independently from their belonging to the picture of radionecrosis, many changes have been correlated with different parameters and some, such as peritumoral necroses and macrophage areas, vessel alterations, etc, were put in relation with radiation. They were present in most cases, concentrated around the tumor and more pronounced in two cases treated with misonidazole during radiotherapy. In most cases the isodose curve was reconstructed, showing that the radionecrotic areas received the same or a higher radiation dose. The importance of the peritumoral location of the lesions is discussed. The effect of chemotherapy were much less evident. (no Refs)

3. TUMORS OF THE CEREBRAL AQUEDUCT.

Ho KL

Dept. of Pathology, Wayne State Univ. Sch. Medicine, Scott Hall, 540 East Canfield Ave., Detroit, MI, 48201

Cancer; 49(1):154-162 1982

Two cases of tumor of the cerebral aqueduct are described: Case I is a pilocytic astrocytoma in a 16-year-old girl with a 2-year history of intermittent increase of intracranial pressure. The tumor was completely confined within the lumen of the aqueduct. Case 2 is a subependymoma of a 68-yr-old man. The tumor extended beyond the aqueduct to the periaqueductal gray matter and produced signs and symptoms suggesting normal pressure hydrocephalus. The literature contains 18 other cases of tumor of the aqueduct: 13 gliomas and 5 vascular malformations. All, except one, produced clinical manifestations of generalized hydrocephalus lasting from 20 days to 6 years. The result generally did not correspond to the histologic type of the tumor. Like gliomas of the brainstem in general, those in the aqueduct tend to occur in childhood and adolescence and affect male more than female patients. (Author abstract) (30 Refs)

NEURONAL CELL AND PRIMITIVE BIPOTENTIAL PRECURSOR CELL TUMORS

4. IMPROVED RELAPSE-FREE SURVIVAL IN MEDULLOBLASTOMA UTILIZING MODERN TECHNIQUES.

Norris DG, Bruce DA, Byrd RL, Schut L, Littman P, Bilaniuk LT, Zimmerman RA, Capp R, Hoffman HJ, Wilson CB

Cleveland Clinic Foundation, 9500 Euclid Ave., Cleveland, OH, 44106

Neurosurgery; 9(6):661-664 1981

The impact of microsurgery and computed tomography (CT) was studied in two groups of patients with medulloblastoma treated by the same surgical and radiotherapy (RT) groups. Group 1 was treated before, and Group 2, after December 1974, when microsurgery was introduced. Groups 1 and 2 each contained 11 evaluable patients of both sexes; av ages at diagnosis were 7 yr, 2 mo and 10.0 yr, respectively. Range of ages was 2 yr, 10 mo to 12 yr, 10 mo (Group 2) and 3 yr, 5 mo to 19 yr, 1 mo (Group 2). The dose of RT was similar in both groups. Six children in Group 1 and seven in Group 2 received chemotherapy, with the same agents used for same period of time. Surgical procedures in Group 1 consisted of biopsy (1), subtotal resection (7), total resection (3), compared to 0, 0, and 11, respectively, in Group 2. Mean relapse free survival of 50 mo in Group 2 was significantly greater (p less than or equal to 0.001) than the 42 mo in Group 1. Efforts to minimize tumor burden by total resection did not increase postoperative morbidity or mortality. Relative impact of CT scan, total resection, and increased focus for RT on improved outcome are discussed. (9 Refs)

5. EFFECT OF PTC ON NEUROBLASTOMA (MEETING ABSTRACT).

De Bernardi B, Pastore G, Carli M, Ceci A, Mancini A, Tamaro P

No affiliation given

Third NCI-EORTC Symposium on New Drugs in Cancer Therapy, October 15-17, 1981, Brussels, Belgium European Organization for Research on Treatment of Cancer; A64 1981

PTC (peptichemio) was utilized as initial therapy following diagnosis in 80 children with non-localized neuroblastoma. Of the 67 evaluable patients (21 stage III, 41 stage IV and 5 stage IV-S), 51 had measurable lesions allowing to evaluate PTC activity; objective tumor responses to the drug were recorded in 45 of these 51 cases (88.2%): 5/5 stage III, 37/41 stage IV, 3.5 stage IV-S. Complete remissions (CRs) were obtained in 7 patients (13.7%), partial remissions (PRs) in 32 (62.7%), OIs in 6 (11.8%). Four patients (7.8%) had either no tumor change, or tumor progression. There have been two early drug-related deaths (3.9%). Stage III and IV patients responding to PTC were then treated by irradiation + vincristine (VCR), followed by cycles of a combination of adriamycin (ADR), VCR, CYT. Stage IV-S patients received no furth er therapy. Thirteen of 21 stage III (61.9%), 5 of 41 stage IV (12.2%) and 4 of 5 stage IV-S (80%) are presently alive from 19 to 48 mo (median 27 mo). PTC is an effective agent in advanced neuroblastoma. However, the results of this report do not indicate that its addition to a 'standard' treatment, at least in the schedule adopted in this protocol, has improved the final outcome of children with non-localized disease. (no Refs)

MESODERMAL TUMORS OF THE CNS

6. CT OF MENINGIOMAS ON THE POSTERIOR SURFACE OF THE PETROUS BONE.

Valavanis A, Schubiger O, Hayek J, Pouliadis G
Dept. Diagnostic Radiology, Univ. Hosp. Zurich, Ramistrasse 100, CH-8091 Zurich, Switzerland
Neuroradiology; 22(3):111-121 1981

A detailed analysis of the CT findings in 16 surgically verified cases of meningioma of the posterior surface of the petrous bone is presented. The results indicate that a correct preoperative diagnosis is possible in almost every case. Frequently occurring specific CT criteria for meningioma of the posterior surface of the petrous bone include: hyperdense, homogeneously enhancing, extra-axial, CPA mass; inverse relationship between precontrast attenuation value and degree of contrast enhancement of the tumor; oval shape; obtuse angle between lateral tumor border and posterior surface of petrous bone, and evidence of transcisternal supratentorial tumor extension. Infrequently occuring specific CT criteria include: tumor calcification; hyperostosis or exostosis of the posterior surface of the petrous bone; a comma-shaped tumor configuration in cases with transtentorial tumor extension. Oxygen CT cisternography is the most sensitive and reliable technique for detecting small tumors. The CT differential diagnosis of meningioma of the posterior surface of the petrous bone is discussed. (Author abstract) (38 Refs)

7. NEW EMBOLIZATION METHOD USING ESTROGEN FOR DURAL ARTERIOVENOUS MALFORMATION AND MENINGIOMA.

Suzuki J, Komatsu S
Div. Neurosurgery, Inst. Brain Diseases, Tohoku Univ. Sch. Medicine, 5-13-1 Nagamachi, Sendai, 982, Japan
Surg Neurol; 16(6):438-442 1981

For the treatment of dural arteriovenous malformations, conjugated estrogens were infused continuously through a cannula inserted into the external carotid artery. In six of eight patients, therapeutic effects such as total or partial disappearance of the nidus were observed. The same method was employed to occlude the feeders of meningiomas in three patients to reduce bleeding during the operations. The histological findings from the surgically extirpated meningioma are described. (Author abstract) (6 Refs)

SECONDARY TUMORS OF THE CNS

8. RELATIVE VALUE OF COMPUTED TOMOGRAPHY AND HYPOCYCLOIDAL TOMOGRAPHY IN THE DIAGNOSIS OF PITUITARY MICROADENOMA: A RADIO-SURGICAL CORRELATIVE STUDY.

Bonafe A, Sobel D, Manelfe C
Dept. Neuroradiology, Centre Hospitalier Universitaire de Purpan, Toulouse Cedex, France
Neuroradiology; 22(3):133-137 1981

The relative value of a second generation CT scanner and complex motion polytomography are compared in 36 patients undergoing transsphenoidal surgery due to clinical and biological evidence of pituitary hypersecretion. CT findings of focal glandular hypodensity in 17 patients and upward convexity of the sellar contents in 15 patients suggested the presence of a pituitary microadenoma. Complex motion tomographic findings suggesting a microadenoma were found in 21 of 32 cases and included bulging of the sellar floor or localized thinning of the lamina dura. Selective transsphenoidal adenomectomy was performed on 34 of the 36 patients and the preoperative location based on CT scanning data was positively correlated with surgical results in 75% of the cases. When there is a strong clinical suspicion of pituitary hypersecretion both CT and polytomography may suggest the existence and location of a microadenoma. CT should be the radiographic technique of choice since it produces accurate information as to the size and density of the pituitary gland. (Author abstract) (27 Refs)

9. PROLACTINOMA: A QUESTION OF RATIONAL TREATMENT.

Edwards CR, Feek CM
Western General Hosp., Univ. Edinburgh, Edinburgh EH4 2XU, Scotland
Br Med J; 283(6306):1561-1562 1981

Incidence of prolactinomas, pathophysiology, tests for differential diagnosis, clinical course, and therapeutic measures are discussed. A policy for long term management is sought. Prolactinomas appear to develop as a primary pituitary disorder and not secondary to hypothalamic disease. Most women with prolactinomas present in early reproductive life with various types of menstrual abnormalities and infertility; signs may be galactorrhea or visual impairment. Men present later with impotence and sometimes obesity. Diagnosis is confirmed when serum prolactin is consistently high and an enlarged pituitary fossa is observed on plain skull radiography. Macroadenomas that extend above the sella to affect optic pathways require transsphenoidal microsurgery with postoperative external radiotherapy and administration of bromocriptine if hyperprolactinemia persists. Bromocriptine is the treatment of choice for macroprolactinomas without suprasellar extension and for microprolactinomas, which are associated with consistently high serum prolactin and inhibited response to dynamic testing. Bromocriptine therapy should be avoided during pregnancy if possible. A rational plan for management of prolactinomas cannot be made until more is learned about the clinical course. (35 Refs)

10. SURGERY OF THE PITUITARY GLAND.

Tindall GT, Tindall SC
Dept. Neurosurgery, Emory Univ. Sch. Medicine, Atlanta, GA
Curr Probl Surg; 18(10):610-679 1981

Diagnostic and therapeutic advances in the management of pituitary disorders and effects of these developments on the treatment of endocrine-sensitive breast and prostate cancers are reviewed. Specific topics covered include pituitary gland anatomy; incidence, pathology, and clinical features of pituitary tumors; diagnostic endocrinologic and neuroradiologic studies; and treatment protocols for the following specific pituitary abnormalities: asymptomatic enlarged sella turcica and empty sella syndrome, tumors causing mass effects, prolactin-secreting adenomas, acromegaly, and Cushing's disease or Nelson's syndrome. Steps in transsphenoidal and and transcranial pituitary surgery, postoperative management, and complications of surgery are discussed. Management of residual or recurrent adenomas, recurrent or persistent hypersecreting tumors, and recurrent nonfunctional tumors is also described. Indications for hypophysectomy in breast and prostate cancer are discussed along with hypophysectomy techniques and postoperative patient management. (162 Refs)

OTHER THERAPY OF CNS MALIGNANCIES

11. PHOTORADIATION THERAPY IN THE TREATMENT OF MALIGNANT BRAIN TUMORS: A PHASE I (FEASIBILITY) STUDY.

Laws ER, Cortese DA, Kinsey JH, Eagan RT, Anderson RE, Chou SN

Dept. Neurologic Surgery, Mayo Medical Sch., Mayo Clinic, Rochester, MN

Neurosurgery; 9(6):672-678 1981

A system for the photoradiation of hematoporphyrin derivative (HPD) in brain tissue is described which was used in a Phase I study in five patients with incurable, malignant, parenchymal neoplasms which did not respond to conventional therapy. After rapid iv infusion of HPD (5 mg/kg), the patients were protected from sunlight and bright, artificial light for at least 2 wk. After 48-74 hr, a sterile, single quartz fiber probe was implanted 2 mm into the tumor. The fiberoptic probe was coupled to an argon-pumped continuous wave dye laser. The goal of therapy was to deliver 300 milliWatts of red light (wavelength 630 nanometer), for 45 min. Needle biopsies of the lesions were obtained at the beginning and end of each procedure and each sample was evaluated visually for HPD fluorescence under light at 405 nanometer. No significant adverse reactions have occurred, and further development and research are planned. (28 Refs)

12. PRELIMINARY REPORT ON ANTITUMOR ACTIVITY OF CIS-DICHLORODIAMMINE PLATINUM IN METASTATIC BRAIN TUMORS (MEETING ABSTRACT).

Kolaric K, Roth A, Jelicic I, Matkovic A

Central Institute for Tumors and Allied Diseases, 41000 Zagreb, Yugoslavia

Third NCI-EORTC Symposium on New Drugs in Cancer Therapy, October 15-17, 1981, Brussels, Belgium European Organization for Research on Treatment of Cancer; :A90 1981

In spite of pharmacokinetic studies, which have shown that only cis-platinum (Ci s DDP) traces were found in brain tissue, cytotoxic activity of this drug in primary brain tumors was recently reported. The purpose of our study was to examine whether Cis DDP has also antitumor properties in metastatic brain tumors. Twenty-two consecutive untreated patients with brain metastases recorded by computed axial tomography scans or radionuclide scans plus neurological examinations underwent the treatment. Pathohistology of primaries has shown 6 bronchial, 7 breast, 1 gastric and 1 colorectal carcinoma, furthermore 4 melanomas, 1 soft tissue sarcoma, 1 hypernephroma and 1 carcinoma of suprarenal gland. Cis DDP was administered in the doses of 30mg/m2 body surface daily, 4 days. All the patients received at least 3 cycles and have been evaluated. Objective response (5 complete and 6 partial remissions) was observed in 11 out of 22 patients (response rate 50%). Five stable disease cases were also noted, however, in residual 6 patients, the disease in the brain progressed. Complete response (5+, 6+, 7+ mo) was observed in 3 breast cancer patients, 1 (6 mo) in lung cancer and 1 (7+ mo) in melanoma. Six partial responses (lung, breast, melanoma) lasted 2-5 mo. Antitumor activity of Cis DDP was also noted in extra-cerebral tumor lesions (breast, lung and melanoma patients). Toxicity was moderate but tolerable for the patients. The preliminary results of this study have shown that Cis DDP possesses antitumorigenic properties also in the patients with metastatic brain tumors. (no Refs)

13. SELECTIVE HYPOPHYSECTOMY FOR METASTATIC PAIN. A REVIEW OF ETHYL ALCOHOL ABLATION OF THE ANTERIOR PITUITARY IN A REGIONAL PAIN RELIEF UNIT.

Lloyd JW, Rawlinson WA, Evans PJ

Oxford Regional Pain Relief Unit, Abingdon Hosp., Abingdon, Oxon, England

Br J Anaesth; 53(11):1129-1133 1981

Selective adenohypophysectomy, by the injection of up to 1 ml of absolute alcohol to the pituitary gland, was used to produce pain relief in 25 patients suffering from metastatic cancer. Thirty-five treatments were given and good analgesia was obtained in 74%. The median duration of pain relief was 6-7 wk, although some treatments produced relief for up to 20 mo. The procedure was most successful in relieving bone pain in patients with advanced carcinoma of the breast or prostate. The use of a fine-gauge needle for the intranasal transsphenoidal approach to the gland and the injection of alcohol to the anterior part (pars distalis) of the gland reduced the frequency of the major complications diabetes insipidus (17%) and prolonged visual disturbance (3%). (Author abstract) (13 Refs)

SELECTED PRECLINICAL ASPECTS OF CNS CANCER

14. PROBLEMS OF THE CLASSIFICATION OF TUMORS OF THE NERVOUS SYSTEM AND THE SIGNIFICANCE OF ELECTRON MICROSCOPY.

Zulch KJ

Max-Planck Institut fur Hirnforschung, Ostmerheimer Str. 200, D-5000 Koln 91, W. Germany

Folia Histochem Cytochem (Krakow); 19(3):171-178 1981

Difficulties encountered using electron microscopy (EM) in routine work are related to proper selection of material, duration of the technical process, and the very restricted field of observation. Processes of degeneration in astrocytomas and oligodendrogliomas are more clearly visible using EM. Identification of glioblastoma multiforme is better by light microscopy, which clearly shows the production of intercellular reticular fibers in the real monstrocellular types. In medulloblastoma, EM has contributed to knowledge of the derivation of tumor cells. Two types of pineal tumors can be detected by EM; the World Health Organization had previously classified them differently. Ultrastructure has not contributed significantly to the definition of anaplasia. The blood-brain-barrier in brain tumors and viral pathogenesis have been studied using EM. (36 Refs)

15. ANAPLASTIC HUMAN GLIOMAS GROWN IN ATHYMIC MICE: MORPHOLOGY AND GLIAL FIBRILLARY ACIDIC PROTEIN EXPRESSION.

Jones TR, Bigner SH, Schold SC, Eng LF, Bigner DD

(c/o Bigner) Dept. Pathology, Duke Univ. Medical Center, Box 3156, Durham, NC, 27710

Am J Pathol; 105(3):316-327 1981

The morphologic and biochemical characteristics of human surgical biopsy specimens taken from 17 patients with anaplastic human gliomas and of athymic mouse-grown tumors derived from them were examined. Fourteen were categorized as glioblastoma multiforme, one as an anaplastic astrocytoma, one as a recurrent glioblastoma multiforme, and one as a gliosarcoma. Fifteen of 17 tumors stained positively immunohistochemically for glial fibrillary acidic protein (GFAP), a glial-specific marker. When portions of the 17 surgical biopsy specimens were injected into the flank subcutaneous space of athymic mice, 16 produced tumors; different portions of a single biopsy specimen were used to establish three separate tumor lines; in toto, 18 tumor lines were established. Mouse-borne tumors contained various proportions of fibrillary and protoplasmic astrocytes, gemistocytes, small anaplastic cells, and multinucleated giant cells. Some were more homogeneous than the human tumors from which they were derived, while others contained a mixed population similar to that of the original biopsy specimen. Of these initial 18 tumors, 16 were stained for GFAP and 14 contained from fewer than 5% to almost 100% GFAP-expressing cells. Ten of the tumor lines were studied in serial passage, several demonstrating increased cellularity with increased passage. GFAP expression was followed through serial passage, and 7 of 10 tumor lines continued to express it, often in reduced amounts, and 2 of 10 ceased expression, one (the gliosarcoma) never having expressed it. These data demonstrate that while athymic mouse-borne human anaplastic gliomas retained some features of the human tumors from which they were derived, they varied from one another morphologically. These mouse-borne tumors also continued to evolve, often changing their levels of GFAP and demonstrating increased cellularity with passage. (Author abstract) (34 Refs)

16. CLONOGENIC CELL ASSAY: ANALYSIS OF HUMAN BRAIN TUMORS (MEETING ABSTRACT).

Gerosa MA, Rosenblum ML, Dougherty DV, Wilson CB

Brain Tumor Research Center, University of California, San Francisco, CA, 94143

Third NCI-EORTC Symposium on New Drugs in Cancer Therapy, October 15-17, 1981, Brussels, Belgium European Organization for Research on Treatment of Cancer; :A24 1981

Recently we developed an in vitro clonogenic assay for human brain tumors. Colonies grew from greater than 90% of primary and metastatic tumor samples cultured, and were characterized with histochemical and immunobiological methods. To date, cells from 37 tumors have been analyzed for in vitro cell sensitivity to carmustine (BCNU). A correlation between culture and clinical results was obtained for 21 samples. The predictive accuracy in 13 patients never previously treated with nitrosoureas was 70% for sensitivity and 100% for resistance, similar to results from other stem-cell assays and to the estrogen receptor assay for breast carcinoma. Problems inherent in this assay have been addressed: viable, clonogenic tumor cells representative of the cells in the solid tumor were obtained using enzyme disaggregation methods. Short-term culturing of cells increases both the colony forming efficiency and the number of cells available for drug testing, BCNU sensitivity remains the same for cultured and original cells. Effects of tumor cell heterogeneity have been evaluated by analyzing histologically distinct specimens from individual tumors. BCNU dose-response curves were generally similar among different specimens. However analysis based on single drug doses might be misleading. Analysis of data from patients harboring recurrent tumors suggests that drug delivery in situ will limit the predictive value of a sensitive response, but will not affect the predictive value of resistance. (no Refs)

17. HUMAN MALIGNANT GLIOMAS ASSOCIATED ANTIGENS (MEETING ABSTRACT).

de Muralt B, De Tribolet N, Diserens AC, Carrel S

Ludwig Institute for Cancer Research, 1066 Epalinges, Switzerland

UICC Conference on Clinical Oncology, October 28-31, 1981, Lausanne, Switzerland. International Union Against Cancer 131 pp., 1981.

Hybridoma cells have been derived from a fusion between mouse myeloma cells P3X63 Ag/8 and spleen cells from a mouse immunized with whole cells of a human malignant glioma line LN-18. Three Hybrids were selected and cloned by limiting dilution. The specificity of the 3 monoclonal antibodies was investigated by an indirect antibody-binding radioimmunoassay on a panel of cell lines, short term cultures and fresh cell suspensions, derived from 37 human malignant gliomas, 3 meningiomas, 1 retinoblastoma, 1 medulloblastoma, normal fibroblasts and peripheral blood lymphocytes, as well as 18 cell lines from non gliogenous neoplasms. The monoclonal antibody GE2 bound to 17/18 gliomas cell lines, 16/17 short term glioma cultures and 1/2 fresh cell suspensions of gliomas. BF7 bound to 13/18, 15/17 and 1/2 respectively. They did not bind to any other cells and appear to react with common malignant glioma antigens. The third monoclonal antibody, C-G12, appears to react with a neural crest associated antigen since it was found to bind to 17/37 gliomas tested, 1 neuroblastoma, 1 medulloblastoma and 5/5 melanomas. Absorption with normal adult and fetal brain homogenate did not modify the binding capacity of GE2 and BF7 but totally abolished the binding activity of C-G12. (no Refs)

18. THE USE OF MONOLAYER CULTURES AND MULTICELLULAR SPHEROIDS DERIVED FROM HUMAN BRAIN TUMORS AS MODELS FOR IN VITRO CHEMOSENSITIVITY MEASUREMENT AND DRUG SCREENING (MEETING ABSTRACT).

Darling JL, Oktar N, Thomas DG, Cooper G

Institute of Neurology, Queen Square, London WCIN 3BG, England

Third NCI-EORTC Symposium on New Drugs in Cancer Therapy, October 15-17, 1981, Brussels, Belgium European Organization for Research on Treatment of Cancer; :A82 1981

Existing systems for screening new drugs for cytotoxic activity and biopsy material for individualized chemotherapy suffer from a number of disadvantages. Using monolayer cultures and multicellular spheroids produced from a range of human primary and secondary brain tumors we have examined the patterns of chemotherapeutic response in vitro. Surgical biopsies were minced and disaggregated with collagenase. The resultant cell suspension was diluted to 5 x 10(5) cells/ml and either inoculated into conventional tissue culture flasks (monolayer assay) or into flasks coated with 0.5% agar (multicellular spheroid assay). Monolayer cultures were assayed for drug sensitivity using 35S methionine uptake as measured by scintillation autofluorography. Spheroids (mean diameter 1.4 x 106um(3)) were transferred into individual agar coated wells of a microtitration plate. At least 10 spheroids were used for each trial. They were exposed to graded concentrations of drugs for 24 hr at 37C. The spheroids were measured daily using a calibrated eyepiece micrometer for a ten-day period following drug removal and the growth delay calculated. Spheroids were also disaggregated after drug treatment and the colony forming efficiency in soft agar was determined. Spheroids showed a dose dependent relationship with both relative growth delay and cell survival. However, with both assay methods, there was considerable heterogeneity in response both between tumors of similar histopathology. A relationship between the clinical response of a group of patients with malignant glial tumors and the cellular sensitivity in monolayer assay has been noted and may provide the basis for individualized chemotherapy and a rational basis for the use of new drugs. (no Refs)

19. DISTRIBUTION AND LIFE HISTORY OF RAT BRAIN TUMORS INDUCED BY HUMAN ADENOVIRUS TYPE 12 IN THEIR EARLY STAGES OF THE ONCOGENESIS.

Shinozaki Y
2nd Dept. Pathology, Okayema Univ. Medical Sch., 2-5-1, Shikata-cho, Okayama, Japan
Pathol Res Pract; 172(4):330-340 1981

Newborn rats were intracranially inoculated with human adenovirus Type 12 within 24 hr after birth and their brains were sequentially investigated by conventional histological techniques and autoradiography to clarify the early process of tumor growth. At the end of the 2nd wk atypical cells having bizarre configuration first appeared singly in the tapetum. From the end of the 3rd wk small clusters of slightly atypical subependymal cells ('abnormal clusters') appeared in the subependymal area. From the end of the 4th wk a few 'microtumors' showing compact nodular growth of atypical glial cells were observed among the 'abnormal clusters'. These early neoplastic changes in the rat brains had close relationship to subependymal cells. The perinatal subependymal cells showed most dense distribution in the subependymal area of lateral ventricle with open ventricular space ('open ventricular area') especially in the region of anterior horn. In contrast, the microtumors and the enlarged tumors were recognized much more in number in the subependymal area of bulbus olfactorius and tapetum where ventricular cavities closed in the young period of maturation ('closed ventricular area'). 'Abnormal clusters' were located in both of the areas with more preponderance in the open ventricular area. The reasons for this discrepancy of occurrence were discussed from the viewpoint of environmental factors. Subsequent investigation revealed that the av number of microtumors, after reaching its peak at the end of the 5th wk, diminished gradually and, finally, only one or two enlarged tumors were found per each tumor-bearing animal. The mechanisms for this phenomenon are open to further investigation. (Author abstract) (21 Refs)

REVIEWS

20. INTERSTITIAL IRRADIATION OF BRAIN TUMORS: A REVIEW.

Bernstein M, Gutin PH

(c/o Gutin) Editorial Office, 350 Parnassus Ave., Suite 807, San Francisco, CA, 94117

Neurosurgery; 9(6):741-750 1981

The general history of clinical interstitial irradiation (IR) for neoplasms is reviewed and the history and current status of IR for brain tumors is discussed. IR has two advantages over teletherapy: radiation delivered at low dose rates and intratumoral placement of sources. The differential cell killing effectiveness is increased by the exposure to low dose rate, compared to high dose rate, irradiation. The computed tomography scanner has revolutionized the use of IR for brain tumors. The fact that trials of IR for brain tumors have been conducted at many centers where it is no long employed is an indication that such tumors are deeply situated. It is stressed that the theoretical advantages of the low dose rate radiation and the intratumoral placement of the source warrant continued study and improvement in this modality. In the authors' institution, primary and recurrent malignant brain tumors have been implanted with removable or permanent 192Ir, 198Au, or 125I sources since 1977. Doses to the periphery of the tumors ranged from 3,000 to 20,000 rads. Preliminary results of the study have been encouraging. (175 Refs)

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CNS MALIGNANCIES

Diagnosis, Treatment

SERIES CT18 No. 82/06

JUNE, 1982

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NEUROGLIAL CELL TUMORS

1. PRIMARY MALIGNANT CEREBELLAR ASTROCYTOMAS IN CHILDREN: A SIGNAL FOR POSTOPERATIVE CRANIOSPINAL IRRADIATION.

Salazar OM
Div. Radiation Oncology, Univ. Rochester Cancer Center, P.O. Box 647, Rochester, NY, 14642

Int J Radiat Oncol Biol Phys; 7(12):1661-1665 1981

Therapeutic results and natural history of 13 cases of malignant astrocytoma of the cerebellum (MAC) are reported. Eight cases involved primary pure malignant astrocytomas; five cases

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involved mixed tumors in which the malignant astrocytoma component predominated. All tumors had been surgically and histologically confirmed and had been treated with 60Co irradiation. Seven patients were treated with cra niospinal irradiation (CSI) consisting of 4,500 rads to the whole brain, a 1,000 rad booster to the posterior fossa, and 3,000-4,000 rads to the spinal axis given over five weekly treatments. Six patients received only cranial irradiation (CI); four of these received only partial CI. Median age of all patients was 9.8 yr. Male:female ratio was 1.6. Median survival (MS) was 20 mo. MS for patients receiving CI was 10 mo compared with 48 mo for patients receiving CSI. At reporting time six CSI patients were alive with no evidence of disease; one CI patient was alive with disease. All other patients had died. Five CI patients developed spinal subarachnoid dissemination after a median 9.6 mo. None of the CSI patients developed spinal metastases. Results suggest that MAC should be treated by CSI, rather than by more restricted radiotherapy. (26 Refs)

2. BORON NEUTRON CAPTURE THERAPY IN THE TREATMENT OF GLIOBLASTOMA (MEETING ABSTRACT).

Ashtari M, Brownell GL
Department of Nuclear Engineering, Massachusetts Institute of Technology, Cambridge, MA, 02139
Med Phys; 8(5):736 1981

Boron Neutron Capture Therapy (BNCT) is an alternative technique of radiation therapy, which relies on selective loading of a tumor with a 10B enriched compound and subsequent irradiation with a thermal or epithermal neutron beam. Neutrons are captured in boron nuclei and undergo an (n, alpha) reaction. The resultant charged particles release a tremendous amount of energy in a small distance of 5-10u, comparable to a typical cell diameter, which results in irreparable damage to the cells. To prove the feasibility of BNCT as well s to evaluate the inherent radiation risks involved, we have established animal studies at MIT, MGH, and BWH. The neutron beam for this study is provided by the Medical Facility at the MITR-II which was specifically designed for BNCT. The dosimetry is complicated by the mixed incident radiations (thermal neutrons, incident gamma and fast neutrons), and neutron induced radiations in tissue. To evaluate each of these dose components various dosimetric techniques have been applied through extensive phantom studies. (no Refs)

NEURONAL CELL AND PRIMITIVE BIPOTENTIAL PRECURSOR CELL TUMORS

3. MEDULLOBLASTOMA: IDENTIFICATION AND IMPLICATIONS OF PROGNOSTIC SUBGROUPS (MEETING ABSTRACT).

Kopelson G, Linggood R, Kleinman G
Departments of Radiation Medicine and Pathology, Massachusetts General Hospital and Harvard Medical School, Boston, MA, 02114
UICC Conference on Clinical Oncolcgy, October 28-31, 1981, Lausanne, Switzerland. International Union Against Cancer 131 pp., 1981.

Forty-three medulloblastoma patients seen from 1962-1979 were evaluated for prognostic factors and post-irradiation local control rates as a function of a new histopathologic subclassification scheme (TS equals tumor score, a function of necrosis, desmoplasia, mitoses, and cytoplasmic processes), TM staging, as well as classical clinical parameters. The overall actuarial 5- and 10-yr survival rate was 56% +/-9%. Factors from the literature which previously have had prognostic importance (age, sex) did not affect prognosis in this series. The most significant parameters were TM stage and TS. Survival rates were better for: low T-stage (82% T1, 2 vs 46% T3, 4, P less than 0.02), low M-stage (63% MO, 1 vs 0% M2, 3 P less than 0.03), and favorable histopathologic subtype (81% TS less than or equal to 5 vs 41% TS greater than or equal to 6, P less than 0.05). Posterior fossa local control rates post-irradiation were a function of T-stage and histology. Combining T-stage and TS resulted in 3 major prognostic and local control groups. Small (T1,2) tumors of favorable histology (TS less than or equal to 5) had a 10 yr survival of 92% with 100% local control; no change from present management is suggested. An intermediate prognosis group with 67% and 70% survival, respectively, demonstrated evidence of an irradiation dose-response relationship for local tumor control; by only increasing the posterior fossa dose for these patients, improved survival may result. In the poor prognosis group with 42% survival, increasing the posterior fossa dose to greater than or equal to 5000 rad did not increase local tumor control. Patients for future adjuvant chemotherapy or radiosensitizer trials might be selected from this poor risk group of patients with large and/or necrotic tumors. This paper identifies prognostic subgroups based upon histology and TM staging in medulloblastoma patients, which potentially may be utilized to improve therapeutic results, and confirms the value of staging CNS malignancies. (no Refs)

4. CHEMOTHERAPY OF NEUROBLASTOMA (MEETING ABSTRACT).

Bessho F, Fujio M, Mizutani S, Kaku H, Hayashi Y
Dept. Pediatrics, Faculty Medicine, Univ. Tokyo, Bunkyo-ku, Tokyo 113, Japan
Shoni Gan; (16):19-22 1981

Chemotherapy consisting of the administration of 150 mg of cyclophosphamide (CPA) per m2 for 7 consecutive days and 35 mg of adriamycin (ADM) per m2 on day 8 was used to treat 11 patients with neuroblastoma, aged 1 yr and 6 mo to 14 yr and 7 mo (8 males, 3 females). The primary site was the abdomen, mediastinum, neck and pelvic cavity in six, three, one and one patient, respectively. The stage of five, three, three and one of the malignancies was IIIC, IIIB, IIIA and IIB, respectively. Rapid tumor regression was seen in eight of the nine patients whose response was evaluable. In most of the patients, the tumor disappeared after 1 to 27 courses. After 4 mo, a complete, partial and mixed response or progressive disease was seen in seven, two and two patients, respectively. Five of the patients died 4 to 20 mo after diagnosis and six were still alive 3 to 54 mo after diagnosis. In one 3-yr and 2-mo-old girl with Stage IIIB neuroblastoma of mediastinal origin, the tumor regressed after treatment with CPA and ADM. The residual tumor was partially resected and radiotherapy was conducted. About 1 yr later, a new tumor appeared, and thoracotomy was performed because of hydrothorax of the left chest. Biopsy revealed that most of it was neuroblastoma, and the tumor enlarged rapidly shortly after surgery. After chemotherapy with Cis-platinum and VM-26 (epipodophyllotoxin; NSC, 122819) along with radiotherapy of the tracheal bifurcation, the tumor shrank, the respiratory difficulty was relieved and lymph node distention disappeared or decreased. The peculiar side effect of tetany was seen after the fourth course of therapy, the concentration of Ca and Mg in the serum being 6.8 mg/dl and 0.6 mg/dl, respectively. Another side effect was marked myeloid inhibition, and the drug was thought to have an immunosuppressive effect. (no Refs) (In JPN)

MESODERMAL TUMORS OF THE CNS

5. PRESENCE OF SEX STEROID HORMONE RECEPTORS IN MENINGIOMA TISSUE (MEETING ABSTRACT).

Gomez F, Schnegg JF, Lemarchand-Beraud T, De Tribolet N
Department de Medecine, Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland
UICC Conference on Clinical Oncology, October 28-31, 1981, Lausanne, Switzerland. International Union Against Cancer 131 pp., 1981.

Meningiomas in women develop preferentially during luteal phase and pregnancy; in men they are 2-4 x less frequent. This suggests a role for sex hormones in the growth of these tumors. To ascertain the possibility that sex hormones may act directly on meningioma tissue, we looked for the presence of receptors to estrogens (ER), progesterone (PgR), and androgens (AR) in cytosol preparations from 5 consecutive cases of each sex. Receptors were quantified by saturation analysis of displaceable binding to cytosol of 3(H)-estradiol, promegestrone, or-5, alpha dihydrotestosterone (for ER, PgR and AR respecitively), in the 5 x 10(-12)-5 x 10(-9) M final dilution range. No ER were detected in any of the 10 cases studied, in contrast to published data PgR were found in 2 women, one of them post-menopausal and the other one operated upon during follicular phase, and in 2 men, one with borderline-low plasma testosterone, and the other one with bilateral gynecomastia. Three other women (post-menopausal) and 3 other men had no PgR. AR were found only in 2 post-menopausal women who had no PgR. No receptors were found in any of the 3 non-meningioma brain tumors used as controls. The meaning of the presence of PgR or AR in regards to the sexual state of these patients needs clarification. The existence of PgR or AR in some meningiomas makes it possible that these tumors be influenced for growth by gestagens or androgens. (1 Ref)

TUMORS OF THE CRANIAL AND SPINAL NERVE ROOTS

6. ANTERIOR DECOMPRESSION OF THE SPINE FOR METASTATIC EPIDURAL CORD COMPRESSION: A PROMISING AVENUE OF THERAPY?

Siegal T, Siegal T, Robin G, Lubetzki-Korn I, Fuks Z
Dept. Oncology, Hadassah Univ. Hosp., P.O. Box 12000, Jerusalem 91120, Israel
Ann Neurol; 11(1):28-34 1982

The results of 11 anterior decompressions of the spine performed in nine patients with metastatic epidural tumors are reported. No patient deteriorated after surgical intervention. Of eight patients who were previously nonambulatory or paraplegic, seven were ambulatory 30 days following surgery. One patient improved from paraplegia to antigravity muscle function but remained nonambulatory. Two patients did not show improvement in muscle strength but maintained stable neurological status and ambulation. Six patients with bladder/bowel dysfunction regained normal function. Rate of recovery varied from patient to patient and was positively correlated with duration of neurological deficit prior to surgery. Neurological recovery occurred independently of postoperative radiotherapy since improvement was evident prior to radiotherapy. Rate of recovery and duration of ambulation did not differ between four patients in whom surgery was not followed by radiotherapy and in those who completed postoperative irradiation. Tapering high dose dexamethasone did not affect improvement in any patient. All patients enjoyed lasting pain relief immediately after surgery. Five patients have died. Four patients are alive and ambulatory, one 20 mo and two 10 mo after surgery; the fourth required a second operation and has been ambulatory for 5 mo. Of those who died, three survived less than 6 mo and succumbed to generalized metastases. (19 Refs)

TUMORS OF THE LYMPHORETICULAR SYSTEM AND BLOOD VESSELS

7. CEREBELLAR HEMANGIOBLASTOMAS.

Sung DI, Chang CH, Harisiadis L

Dept. Radiation Oncology, Allegheny Valley Hosp., 1301 Carlisle St., Natrona Heights, PA, 15065

Cancer; 49(3):553-555 1982

Between 1950 and 1976, 24 patients with cerebellar hemangioblastomas received postoperative radiation therapy. In retrospect, the low-dose radiotherapy that was practiced in the 1950s and early 1960s has been associated with inferior survival rates. Since 1963 and with increased awareness of the effects of radiotherapy, patients receiving high-dose irradiation postoperatively have generally survival longer. Postoperative radiotherapy is used whenever the neoplasm has not been totally excised. This is more likely to occur with solid hemangioblastoma and neoplasms arising in the brain stem. In addition, radiotherapy should be used when the tumor recurs after total excision. The recommended dose is in the range of 4,500-5,000 rad in 4 1/2-5 weeks. (Author abstract) (11 Refs)

SECONDARY TUMORS OF THE CNS

8. CORTICOLIPOTROPIN IMMUNOREACTIVITY IN SILENT CHROMOPHOBE ADENOMAS: A LIGHT AND ELECTRON MICROSCOPIC STUDY.

Hassoun J, Charpin C, Jaquet P, Lissitzky JC, Grisoli F, Toga M

Laboratoire d'Anatomie Pathologique et de Neuropathologie, 27, Bd Jean Moulin, 13885 Marseille Cedex V, France

Arch Pathol Lab Med; 106(1):25-30 1982

Twenty silent human pituitary adenomas were morphologically studied. Immunoperoxidase methods showed numerous adrenocorticotropic hormone-immunoreactive tumor cells in 14 cases by light microscopy and in one additional case by electron microscopy. Three of these cases were positive for beta-endorphin and one for beta-lipotropin by electron microscopy. These immunoreactions were found in undifferentiated tumors as well as in oncocytic adenomas, and could not be related to the presence of basophils by light microscopy. The peptides so detected in silent adenomas may have no biological activity and may correspond to common precursor molecule subunits. (Author abstract) (35 Refs)

9. THE CLINICAL IMPLICATIONS OF DNA CHARACTERISTICS IN HUMAN PITUITARY TUMOUR DISEASE.

Anniko M, Holm LE, Tribukait B, Werner S, Wersall J
Dept. Otolaryngology, Karolinska Hosp., S-104 01 Stockholm, Sweden
Acta Otolaryngol [Suppl] (Stockh); (379):21-28 1981

DNA analysis was performed in 29 cases of various endocrinological types of human pituitary tumors. The degrees of ploidy and proliferation, expressed as the proportion of cells in S phase, were determined. In 12 cases (41%) aneuploidy occurred. The proportion of aneuploid cells in these tumors was very high, in general around 95% measured. The aneuploid group of pituitary tumors showed a large variation of the percentage of cells in S-phase (range: 3.3-13.7%; mean: 8.3 +-5.3) in contrast to diploid tumors which showed a considerably smaller variation (range: 3.4-8.8%; mean 5.5 +-2.1). Patients with aneuploid tumors had a mean age at operation of 42.8 +-11.1 yr in contrast to 51.5 +-13.8 yr for patients with diploid tumors. Aneuploidy occurred more frequently in tumors causing acromegaly with a concomitant secretion of GH and PRL than in other endocrinological types of tumors. Patients with aneuploid tumors had a mean case history of 2.9 +-1.9 yr, as compared to 10.5 +-4.9 yr for patients with diploid tumors. In many cases, tumors with an aneuploid DNA pattern caused a high clinical activity of acromegaly. (Author abstract) (28 Refs)

10. EXPERIENCE WITH SELECTIVE VENOUS SAMPLING IN DIAGNOSIS OF ACTH-DEPENDENT CUSHING'S SYNDROME.

Drury PL, Ratter S, Tomlin S, Williams J, Dacie JE, Rees LH, Besser GM
Dept. Endocrinology, St. Bartholomew's Hosp., London EC1A 7BE, England
Br Med J; 284(6308):9-12 1982

Twenty-three patients with ACTH-dependent Cushing's syndrome were subjected to selective venous catheterization and sampling for ACTH on a total of 26 occasions. Out of 10 patients with pituitary-dependent disease, 9 had raised ACTH concentrations in one or both high internal jugular vein samples. Eight patients had 11 proved sites of ectopic hormone production: of these, 6 were correctly identified by the sampling technique, and in 4 of them this was the only accurate method of localization. The results of one catheterization were misleading, and on 10 occasions they were inconclusive; five patients remained undiagnosed by any method. Overall, 15 of the 26 catheterizations provided diagnostically valuable information. Selective venous catheterization and sampling for ACTH is effective in confirming a pituitary source of the hormone and may be valuable in locating the source of ectopic ACTH production in some cases. (Author abstract) (21 Refs)

11. TRANSSPHENOIDAL MICROSURGERY FOR PROLACTIN-SECRETING PITUITARY ADENOMAS: RESULTS IN 100 WOMEN WITH AMENORRHEA-GALACTORRHEA SYNDROME.

Faria MA, Tindall GT
Section Neurological Surgery, Emory Univ. Clinic, 1365 Clifton Road, N.E., Atlanta, GA, 30322
J Neurosurg; 56(1):33-43 1982

The authors present the results of transsphenoidal microsurgery in 100 women with the amenorrhea-galactorrhea syndrome caused by pituitary adenomas associated with hyperprolactinemia (prolactinomas). As the surgical results were closely related to the preoperative levels of serum prolactin, the patients were divided into two groups: Patients with preoperative prolactin less than 200 ng/ml (Group 1), and those with preoperative prolactin greater than 200 mg/ml (Group 2). The results in Group 1 (72 patients) were significantly better. In this group 56 (78%) patients regained normal menstrual cycles, and 55 (76%) had return of elevated prolactin levels to normal following surgery. In Group 2 (28 patients), however, only 11 (39%) resumed normal menstrual periods postoperatively, and 13 (46%) had return of elevated prolactin levels to normal. There was good correlation between tumor size and the preoperative level of prolactin. Of the 72 women in Group I, 58 (81%) had tumors less than 1 cm (microadenomas), whereas of the 28 women in Group 2, only 4 (14%) had tumors of that size. All patients with visual field deficits preoperatively improved or had a normal visual examination postoperatively; none was made worse by surgery. Four patients (3 in Group 2) have required additional surgery and/or irradiation. In the last six patients of the series, contrast-enhanced coronal computerized tomography slices made with the updated General Electric scanner detected five microadenomas. Considering that a relatively high percentage of sellar polytomograms are negative in patients with proven microadenomas (that is, only 40 of 72 patients in Group 1 had abnormal polytomography), it is likely that sellar polytomography will significantly decrease in importance in the diagnostic work-up of these patients. The authors provide a rationale for transsphenoidal microsurgery in these patients as opposed to other forms of management, such as bromocriptine therapy and irradiation. (Author abstract) (58 Refs)

OTHER THERAPY OF CNS MALIGNANCIES

12. CISPLATINUM IN RECURRENT BRAIN TUMORS (MEETING ABSTRACT).

Khan AB, D'Souza BJ, Wharam MD, Sinks LF, Woo S, McCullough D, Leventhal BG

Johns Hopkins Oncology Center, Baltimore, MD, 21205

UICC Conference on Clinical Oncology, October 28-31, 1981, Lausanne, Switzerland. International Union Against Cancer 131 pp., 1981.

Twenty-two patients with brain tumors were treated initially with surgery, radiotherapy and/or adjuvant chemotherapy. At recurrence, demonstrated by computed tomographic (CT) scan, they were given cisplatinum 60 mg/m2 iv/d x 2 days every 3 wk. Five patients received only 1 course and are not evaluable for response. Tumor types included 7 glioma, 6 ependynoma, 1 dysgerminoma, 1 teratocarcinoma, 1 pinealoma and 1 small cell tumor. Toxicity was graded by CALGB criteria. The number of patients showing grade 3-4 toxicity were: platelets 7; white count 4; renal 3; gastrointestinal 9. Nine out of eleven patients tested showed high frequency hearing loss. Acute fluid retention with low serum electrolytes and some serious, but reversible changes in mental status were seen in 13 patients. In summary, platinum appears active in a spectrum of brain tumors and should be further studied to therapeutic efficacy. Toxicity is manageable. Severe fluid and electrolyte problems are more common in patients with brain tumors. (no Refs)

OTHER CLINICAL ASPECTS OF CNS CANCER

13. VENTRICULOGRAPHY WITH A NEW WATER SOLUBLE NONIONIC CONTRAST MEDIUM - IOPAMIDOL.

Signorini E, Ciorba E, Pelliccioli GP, Caputo N, Cianciulli E, Floridi P, Piccinin GL
Servizio di Neuroradiologia, Ospedale Generale Regionale, 96100 Perugia, Italy
Radiol Med (Torino); 67(12):957-964 1981

Twenty-five ventriculographies (VG) were performed in 24 patients (4-72 yr old, 13 males and 12 females) with iopamidol [200 mgI/ml (1 case), 300 mg I/ml (2 cases), and 370 mg I/ml (22 cases)] as contrast medium. Neither medication nor double contrast medium were used; iopamidol was not removed at the end of VG. Iopamidol gave excellent VG pictures; the highest concentration was the most effective and the side-effects indicated low neurotoxicity. Side-effects were observed in three patients. One patient had headache and nausea starting 10 min after the test and lasting 4 hr. A second patient had headache, nausea, and vomiting that started 3 hr after the test and lasted 5 hr. A third patient had urticaria that started 48 hr after the test and lasted 10 days. Radiologic diagnoses were as follows: neoformation (5), hydrocephalus (3), dilation (7), metastases in posterior cranial fossa (1), periventricular dissemination of pinealoblastoma (1), glioma of optic nerves (1), intraventricular hemorrhage (1), diffuse cerebral atrophy (1), tumor (2), normal (1), and bulbous echinococcus (1), and normal (1). (18 Refs) (In ITA)

14. SERIAL CT BRAIN SCANS AFTER CNS 'PROPHYLAXIS' IN ALL IN CHILDHOOD (MEETING ABSTRACT).

Javier G, Ortega JJ, Manchon Grimalt A
Hospital Infantil de la Seguridad Social Universidad Autonoma, Barcelona, Spain
Sixth Meeting of the International Society of Haematology, European and African Division, August 30-September 4, 1981, Athens, Greece. Hellenic Society of Haematology 409 pp., 1981.

Neurotoxicity due to two different CNS 'prophylaxis' regimens was studied in 30 children with acute lymphocytic leukemia (ALL) through a series of computed tomographic (CT) brain scans at 6, 12, 24 and 36 mo. Group A was given cranial irradiation (2400 r) and it methotrexate (MTX), 6 doses. Group B was given it chemotherapy with MTX and cytosine arabinoside (Ara-C) to a total 10 doses over a 5 mo period. Group A: at 6 mo, 33% showed CT changes: ventricle dilatation and/or subarachnoid spaces widening; 3 patients had moderate periventricular demyelination as well. At 12 mo alterations persisted in only 3, with slight improvement in 2. One patient had cranial hypertension syndrome and reversible coma with features of cerebral atrophy and diffuse demyelination. At 2 yr scans were normal in all other patients. Group B: at 6 mo, 6 out of 15 patients (40%) showed CT findings suggesting demyelination. At 12 mo scans had normalized in 3, alterations persisted in 2 and worsened in 1; another 3 with previous normal scans showed similar alterations: moderate atrophy lesions and multiple calcification were found in one patient who presented an akinetic crisis. At 24 mo, alterations persisted in 4: 2 improved, 1 remained unchanged and 1 worsened. Alterations in CT brain scans were found at least once in 46% of cases. Patients given cranial irradiation showed more frequently changes suggesting atrophy lesions. Those given it polychemotherapy showed mainly images of decreased attenuation; most of these changes revealed as transient. Up to now one patient in each group has presented subacute leukoencephalopathy. We have found no correlations of CT changes with age, cerebrospinal fluid alterations or the previous presence of somnolence syndrome. (no Refs)

15. BRAIN TUMOR EVALUATION USING PET AND RB-82 (MEETING ABSTRACT).

Yen CK, Yano Y, Budinger TF, Friedland R, Derenzo S, Huesman R
Donner Laboratory, University of California, Berkeley, CA
Clin Nucl Med; 6(9S):448 1981

Positron emission tomography (PET) of the brain with rubidium 82 (Rb-82) obtained from a portable generator (Sr-82(25 days)-Rb-82(76 seconds)) was used to evaluate the blood-brain barrier (BBB) integrity of brain tumors in patients. Rubidium is normally excluded from the CNS by the intact BBB. The BBB is disrupted by the tumors and allows entry into the CNS of intravenously administered Rb-82 tracers. Since RB is also rapidly cleared from the blood, high tissue to blood ratio of the Rb-82 tracer is achieved in the regions of BBB disruption. Of 7 patients studied, 6 showed Rb uptake in the lesions. Contrast enhancement on x-ray computed tomography was seen in 4 of the 6 patients. The CT image of the remaining patient, whose lesion did not take up Rb, showed no contrast enhancement. The results of our study show that this technique is a sensitive and accurate method to evaluate the BBB integrity in brain tumor patients. (no Refs)

16. EVOKED POTENTIALS IN THE CLINICAL NEUROSCIENCES.

Greenberg RP, Ducker TB
Div. Neurosurgery, Medical Coll. Virginia, Box 631, MCV Station, Richmond, VA, 23298
J Neurosurg; 56(1):1-18 1982

The use of evoked potentials for the evaluation of disorders of the nervous system has become a most valuable aid to the neurosurgeon and neurologist, often providing information of critical value without recourse to invasive techniques. In order to employ these techniques, it is helpful to understand the principles of evoked potential electrogenesis and the methodology used for analysis of evoked potential clinical data. This article is aimed at providing the clinical neurosurgeon with this type of information and with a review of current clinical applications in this rapidly developing field. (Author abstract) (126 Refs)

17. BRAIN STEM ELECTRICAL RESPONSES IN CEREBELLO-PONTINE ANGLE TUMOURS.

Rosenhall U
Dept. Audiology and Otology, Sahlgren's Hosp., Univ. Goteborg, Goteborg, Sweden
J Laryngol Otol; 95(9):931-940 1981

Thirty patients with cerebello-pontine angle tumors were studied with brain-stem electrical responses (BSER). Twenty-one of the patients had acoustic neuromas. Two other patients had meningiomas, one a lymphoma, one a chordoma, two patients arterio-venous malformations, and two aneurysms in the cerebello-pontine angle. In eight cases no BSER-waves could be evoked. In 13 cases with a Wave V present this wave was significantly delayed in all cases. The inter-aural time difference (IT5) and I-V interval was prolonged in all those cases in which these parameters could be estimated. In nine cases, only the earlier components of the BSER (I and III) could be distinguished although Wave II was often missing. In all 30 cases studied the BSER was pathological, indicating a cerebello-pontine angle lesion. (Author abstract) (14 Refs)

18. EXPERIENCE WITH AN IMPLANTED INFUSION SYSTEM FOR SUSTAINED EPIDURAL NARCOTIC ANALGESIA IN CANCER PAIN (MEETING ABSTRACT).

Coombs D, Saunders R, Gaylor M, Pageau M

Dartmouth-Hitchcock Medical Center, Hanover, NH

UICC Conference on Clinical Oncology, October 28-31, 1981, Lausanne, Switzerland. International Union Against Cancer 131 pp., 1981.

Seven patients with pain related to malignancy who failed to get relief from oral analgesic combinations gave informed consent to participate in this study. Each patient's pain problem was evaluated using battery of psychometric exams for functional activity, depression, and marital adjustment. All patients demonstrated pain secondary to local extension and/or metastasis in association with rectal/colonic adenocarcinoma. Inclusion criteria included a demonstrated 50% reduction in visual pain analogue scale scores with an analgesic duration of greater than 8 hr following a single epidural injection of morphine sulfate (2-5mg) at a spinal level appropriate to the area of pain. Further, this effect had to be repeatable on at least 3 separate occasions. An absence of significant depression (Zung 0.65) was required to minimize the effects of depression upon pain reporting. Seven patients were implanted under sterile operating conditions and have now been followed for periods of 4-6 mo. Each patient had a pliable silastic epidural catheter tunneled laterally, subcutaneously to a rechargable implanted infusion reservoir. Morphine infusion rates of 4-40mg/day have been associated with the following results: 1) It is possible to discontinue most oral analgesics. 2) patients have experienced no sedation or respiratory complications, 3) outpatient control is feasible, 4) reduced narcotic effects on the bowel, and 5) tolerance has been seen at about 1 mo requiring an increase in dosage, however, the quality of pain relief has been uniformly preferable for the patient. This method of cotinuous analgesia appears to have great promise and may be acceptable alternative to neuro-oblative techniques for pain control in the cancer patient. (no Refs)

SELECTED PRECLINICAL ASPECTS OF CNS CANCER

19. HUMAN HYBRIDOMAS FROM MALIGNANT GLIOMAS.

Sikora K, Alderson T, Phillips J, Watson JV
Ludwig Inst. Cancer Res., Hills Road, Cambridge, CB2 2QH, England
Lancet; 1(8262):11-14 1982

Intratumoral lymphocytes from 12 patients undergoing craniotomy for malignant glioma were fused with a specially derived human myeloma line LICR-LON-HMy2. Seventy one stable hybridomas were obtained from 5 of the 12 patients. Such hybridomas had a DNA content equal to the sum of that present in lymphocytes and the parent myeloma. The hybridoma supernatants contained human monoclonal immunoglobulins. Glioma-binding activity was detected in 7 out of the 71 supernatants. These results suggest that malignant gliomas contain a population of B lymphocytes which may be involved in host defense against the tumor. (Autho r abstract) (14 Refs)

20. CHEMOSENSITIVITY OF HUMAN BRAIN TUMORS (MEETING ABSTRACT).

Bogdahn U, Dommasch D, Kappos L, Rohkamm R
Neurological Department, University of Wurzburg, Wurzburg, W. Germany

UICC Conference on Clinical Oncology, October 28-31, 1981, Lausanne, Switzerland. International Union Against Cancer 131 pp., 1981.

With increasing application of chemotherapy towards human malignant brain tumors there is more demand for a rapid and reliable in vitro system predicting the individual tumor response with different therapeutic agents. So far fifteen human malignant gliomas were assayed with a microculture system: tumor cell suspensions were prepared from biopsy specimen, aliquots of 50x10(5) cells were incubated for three days in the presence of various cytostatic agents (Adriamycin, adenine arabinoside, carmustine, cytosine arabinoside, Bleomycin, Cisplatin, Dacarbacin, Methotrexate, Procarbacin, Vincristin, Vepesid, Human Fibroblast/Leucocyte Interferon) and incubated another three days in fresh medium. Incorporation of radiolabelled Leucine, Thymidine and Uridine was measured. Morphological changes of tumor cells after incubation with cytostatic agents were observed in tissue culture slides. Results showed a very individual response of different tumors toward the various agents. The effective concentrations of chemotherapeutic agents ranged within therapeutic levels (0.05-2ug/ml)- a dose related response could be observed in vitro. Although it is too early to draw clinical consequences for the individual therpeutical regimen from these experiments - there is increasing evidence for a good correlation of in vitro results and clinical courses - we expect this method to become a valuable clinical tool to detect 'responders' to chemotherapy among malignant glioma patients. (no Refs)

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CNS MALIGNANCIES

Diagnosis, Treatment

SERIES CT18 No. 82/07

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NEUROGLIAL CELL TUMORS

1. A COMPARATIVE STUDY OF EPENDYMOMAS BY SITE OF ORIGIN.

Marks JE, Adler SJ
Div. Radiation Oncology, Mallinckrodt Inst. Radiology, Washington Univ. Sch. Medicine, St. Louis, MO, 63110
Int J Radiat Oncol Biol Phys; 8(1):37-43 1982

The clinical behavior of irradiated ependymomas (EP) arising from different sites (20 supratentorial, 26 infratentorial, 7 spinal cord, and 8 equina cauda) was examined in 61 patients (34 males, 27 females; 25 adults, 36 children) in relation to EP control, clinical and pathologic incidence of spinal seeding, site of failure, dose response, survival, and neurologic function after treatment with surgery and radiation. Persistent or locally recurrent EP at the primary site of EP origin was diagnosed by reoperation in 10 patients, by autopsy in 7, and by clinical deterioration and/or radiographic study in 17. Ventricular spread outside of the irradiated vol was found by autopsy in two patients and by radiography in two. Spinal cord metastases were diagnosed by laminectomy in one patient, cerebral spinal fluid cytology in one, and autopsy in three. The interval from end of radiation until discovery of persistent or recurrent EP was 50 mo for infratentorial, 24 mo for supratentorial, and 17 for spinal cord or cauda equina EP. For 61 patients followed for 3 or more yr, control of primary EP was best for cauda equina, intermediate for spinal cord and infratentorial, and least for supratentorial EP. Spinal metastases occurred in patients with supratentorial (1) or infratentorial (4) EP. The relationship between nominal standard dose, primary tumor control, and failure by site of EP origin is described. Five- and 10-yr survival rates were highest for cauda equina, intermediate for infratentorial and spinal cord, and least for supratentorial EP. Radiation myelopathy and/or cauda equina syndrome developed 3.5-17 yr after treatment with intrathecal gold in 3/8 patients and 1.5 yr after external spinal irradiation in 1/25. Major surgical complications occurred in two patients. Neurologic deficits, retreatment results, second primary tumors, and causes of death are described. (24 Refs)

2. IMMUNOLOGICAL MONITORING OF PATIENTS AFFECTED BY ANAPLASTIC GLIOMA CONCERNING THE EFFECTS OF SURGERY, RADIO-, AND CHEMOTHERAPY: A PRELIMINARY REPORT.

Servadei F, Parente R, Spagnolli F, Gaist G, Padovani R, Bucci M, Steiner L
Divisione di Neurochirurgia, Ospedale Bellaria, Via Altura 3, Bologna, Italy
Acta Neurochir (Wien); 60(1/2):71-80 1982

The authors studied 24 patients affected by anaplastic gliomas as regards immunology. In all of them the authors evaluated the lymphocyte subpopulation (B and T), firstly by simple lymphocyte count, secondly by studying the rosettes E-total and EAC, thirdly by stimulating the lymphocytes with mitogens phytohemagglutinin-P (PHA), concanavalin A (Con A), and pokeweed mitogen (PWM), and lastly by counting the release of Cr51 in Chang liver cells culture in order to obtain antibody dependent cellular cytotoxicity (ADCC). The parameters were also evaluated after surgery and during conventional radio-chemotherapy with BCNU. Whereas the so-called B-pool seems to be unaffected, the preliminary results show that the T-pool (identified by the E-t rosettes and by responses to PHA, PWM, and ConA) is depressed to a statistically significant degree, if compared with a control group. This depression seems to be related to the tumoral mass, and it is not increased by radio-chemotherapy. In addition, ADCC also seems to be depressed in our glioma patients in comparison with a control group and with a group of bladder cancer patients. (Author abstract) (36 Refs)

NEURONAL CELL AND PRIMITIVE BIPOTENTIAL PRECURSOR CELL TUMORS

3. THERAPEUTIC RESULTS ACHIEVED DURING THE PAST FIFTEEN YEARS IN CASES OF MEDULLOBLASTOMA.

Pichler E, Kogelnik HD, Reinartz G, Karcher KH, Zaunbauer F, Jurgenssen OA, Koos W, Kundi M
Universitats-Kinderklinik, Wahringer Gurtel 74-76, A-1097 Wien, Austria
Strahlentherapie; 157(8):508-515 1981

From October 1964 to December 1979 86 patients with medulloblastoma were craniotomized. Since 1967 38 patients had postoperative radiotherapy, and since 1975 14 patients had additional primary chemotherapy. The quality of radiotherapy was analyzed in a retrograde fashion according to radiation quality, extension of radiation field and radiation dosage. Thus, 11 patients were irradiated in an inadequate, 14 in a suboptimal and 13 in an adequate way. Thirty-seven of 40 patients (2 were lost from observation) who had surgery only died, 1 is alive and free of tumor 14 yr after diagnosis. All 11 patients whose radiotherapy was considered as inadequate (including 1 patient who had cytostatic therapy when in her 3rd relapse) and 12 of 14 patients with suboptimal radiotherapy (including 2 with primary chemotherapy) died. Two patients with suboptimal radiotherapy have survived their diagnosis free of tumor for 9 1/2 and 8 3/4 yr respectively. Two of the 13 patients who had adequate radiotherapy and primary chemotherapy died, 11 (10 of them also treated with primary chemotherapy) have survived for 12 to 66 mo. Two of these 11 patients experienced a relapse recently. These and three additional patients are still on therapy. Adequate radiotherapy of the craniospinal axis plus additional primary chemotherapy seem to bring better chances of survival in this small series thus treated. (Author abstract) (63 Refs) (In GER)

4. INTRATHECAL CHEMOTHERAPY FOR LEPTOMENINGEAL DISSEMINATION OF MEDULLOBLASTOMA.

Edwards MS, Levin VA, Seager ML, Wilson CB
(c/o Editorial Office) Dept. Neurological Surgery, Univ. California, 350 Parnassus Ave., Suite 807, San Francisco, CA, 94117-3690
Childs Brain; 8(6):444-451 1981

Thirteen children or young adults harboring medulloblastoma were treated for leptomeningeal dissemination by intrathecal administration of cytosine arabinoside (AR: 8 patients); AR + methotrexate (MT, 3 patients); and AR + MT + triethylene thiophosphamide (TE, 2 patients). Routes of administration were. 9 ventricular (Ommaya reservoir); 1 lumbar; and 3 both routes. The mean doses administered were 120.5 mg AR (range 36-256), 15 mg MT (range 6-24), and in two patients 170 and 60 mg TE. Patients received an av of 9.4 doses (range 3-23). Single complete responses with AR and TE were of short duration (13 and 4 wk, respectively); four of the patients receiving AR responded with stable disease, but two had received concomitant craniospinal reirradiation with misonida-

zole; one patient receiving TE exhibited stability of disease for 69 wk. MT produced two complete responses of 20 and 112 wk, but two of those receiving MT developed acute encephalopathy. No acute toxicity of AR or TE therapy was recognized. (14 Refs)

5. HISTOLOGIC PATTERNS WITH PROGNOSTIC SIGNIFICANCE IN NEUROBLASTOMA.

Ceccamea A, Bonamico M, Napoleoni M
II Istituto di Anatomia ed Istologia Patologica, Universita di Roma, Viale Regina Elena 324, 00161 Roma, Italia
Tumori; 67(6):605-612 1981

The authors report the results of a statistical study on the correlations of survival in 41 children with neuroblastoma. After pointing out the significance of some clinical data, they emphasize the histological findings that may give an indication of the behavior of the tumor, ie the degree of differentiation and lymphocytic infiltration of the neoplastic tissue. Indeed, statistically significant differences were found between dead and surviving children as regards these findings (p less than 0.001). The authors also point out that the degree of cell differentiation is determined by the number of maturing cells and not by the number of completely mature cells. (Author abstract) (21 Refs) (In ITA)

MESODERMAL TUMORS OF THE CNS

6. STEROID RECEPTOR PROTEINS IN HUMAN MENINGIOMAS.

Tilzer LL, Plapp FV, Evans JP, Stone D, Alward K
Clinical Lab., Kansas Univ. Medical Center, Coll. Health Sciences and Hosp., 39th and Rainbow Blvd., Kansas City, KS, 66103
Cancer; 49(4):633-636 1982

Steroid receptor assays play an important role in determining the efficiency of endocrine therapy for patients with breast cancer. Other tumors could also be hormonally dependent and patients with these tumors might also benefit from endocrine manipulation. Thus, patients with meningiomas were tested for the presence or absence of estrogen and progesterone receptors. The results showed that a majority of meningiomas lacked estrogen receptors but contained large amounts of progesterone receptor. Therefore, it should be possible to use antiprogestin therapy in cases where complete surgical resection of meningiomas is not possible. (Author abstract) (10 Refs)

TUMORS OF THE CRANIAL AND SPINAL NERVE ROOTS

7. BILATERAL ACOUSTIC NEUROMAS: CLINICAL ASPECTS, PATHOGENESIS, AND TREATMENT.

Martuza RL, Ojemann RG, Malis LI
Neurosurgical Service, Massachusetts General Hosp., Boston, MA, 02114
Neurosurgery; 10(1):1-12 1982

The cases of 15 patients (9 female, 14-74 yr old; 6 male, 12-32 yr old) with bilateral acoustic neuromas are described. The technical surgical problems, results of treatment, and complications of this illness are discussed. Eleven of the patients had no family history of neurofibromatosis or CNS tumor, and a spontaneous mutation is considered to be responsible for the initiation of disorders in these patients. Most of the patients were 21 yr old or younger when their symptoms began; they had a more fulminant course and a higher incidence of multiple CNS tumors than those who developed symptoms later. Evidence that 17-beta-estradiol may be an important part of the tumor growth control mechanism is presented, and it may explain why Schwann cell tumors preferentially occur in the vestibular nerve, trigeminal nerve, and spinal sensory nerves. Genetic aspects and potential treatment alternatives of bilateral acoustic neuromas are discussed. (51 Refs)

TUMORS OF THE LYMPHORETICULAR SYSTEM AND BLOOD VESSELS

8. CHEMODECTOMAS ARISING IN TEMPORAL BONE STRUCTURES.

Dickens WJ, Million RR, Cassisi NJ, Singleton GT
Div. Radiation Therapy, J. Hillis Miller Health Center, Box J-385, Gainesville, FL, 32610
Laryngoscope; 92(2):188-191 1982

Eighteen patients with chemodectomas arising in temporal bone structures were evaluated and treated at the University of Florida. Seventeen patients have each been followed a minimum of 3 yr. Patients were retrospectively staged as having 'local' or 'advanced' disease, depending on the presence or absence of bone destruction and/or cranial nerve involvement. Fourteen of the patients received radiation therapy as all or part of their therapy; 6 patients were treated with radiation therapy alone, 3 patients were irradiated immediately postoperatively for residual disease, and 5 patients had radiation therapy for recurrence after operation. They were treated with cobalt-60 radiation with doses ranging from 3760 to 5640 rad. All irradiated patients demonstrated evidence of tumor regression, and none have had tumor recurrence with followup of 3-12 yr. Of the eight patients with cranial nerve paralysis prior to therapy, five had return of function of one or more cranial nerves. One of six patients treated initially with radiation therapy had a complication, while six of eight patients irradiated postoperatively had complications. None of the complications were fatal. Three patients treated by operation for early disease limited to the hypotympanum had the disease controlled for 11-12 yr. Guidelines for the selection of initial therapy are discussed. (Author abstract) (8 Refs)

SECONDARY TUMORS OF THE CNS

9. ADRENOCORTICOTROPIN-SECRETING PITUITARY ADENOMAS ORIGINATE FROM THE ANTERIOR OR THE INTERMEDIATE LOBE IN CUSHING'S DISEASE: DIFFERENCES IN THE REGULATION OF HORMONE SECRETION.

Lamberts SW, De Lange SA, Stefanko SZ
Dept. Medicine III, Univ. Hosp. Dijkzigt, 40 Dr. Molewaterplein, 3015 GD Rotterd am, The Netherlands
J Clin Endocrinol Metab; 54(2):286-291 1982

The reactions to bromocriptine in patients with Cushing's disease was correlated with pathological examination of the pi- tuitary adenomas and the outcome of transsphenoidal oper- ation. Fifteen consecutive patients with Cushing's disease were operated upon, and pituitary tumor tissue was removed. In nine tumors, no neural tissue was present in the adenomas (Group I), but in the tissue removed from the other six pa- tients, argyrophilic nerve fibers coursed freely through the ad- enoma tissue (Group II). In two the these six patients, multiple adenomatous and/or hyperplastic cell nests containing nervous tissue were present, while a localization of tumor tissue in the intermediate lobe of the pituitary gland was evident in three of them. Differences between the two groups of patients are pre- sented. We hypothesize that Cushing's disease in man origi- nates from two different locations. Most of the ACTH-secret- ing pituitary adenomas are located in the anterior part of the pituitary gland and can easily be removed during transsphenoi- dal operation. Part of the ACTH secreting pituitary adenomas are, however, intermediate lobe tumors containing nervous tissue. Multiple microadenomas and/or hyperplastic cell nests can be present in some of these patients, and transsphenoidal operation is less successful. This type of adenoma might be rec- ognized by the demonstration of a suppression of plasma ACTH in response to bromocriptine and a lowered sensitivity to dexamethasone. (28 Refs)

10. CUSHING'S DISEASE: TRANSIENT SECONDARY ADRENAL INSUFFICIENCY AFTER SELECTIVE REMOVAL OF PITUITARY MICROADENOMAS; EVIDENCE FOR A PITUITARY ORIGIN.

Fitzgerald PA, Aron DC, Findling JW, Brooks RM, Wilson CB, For- sham PH, Tyrrell JB
Metabolic Res. Unit, Univ. California,, 1143 HSW, San Francisco, CA, 94143
J Clin Endocrinol Metab; 54(2):413-422 1982

Of 12 patients with Cushing's disease who had successful se- lective microadenoma resection documented by clinical remis- sion and reversal of hypercortisolism, 11 developed postoper- ative hypoadrenalism with deficient adrenal responsiveness to exogenous ACTH. The ACTH and glucocorticoid deficiency was not caused by the surgical procedure or hydrocortisone replacement, since it resolved despite replacement therapy; fur- ther, adrenal insufficiency did not occur in 10 acromegalic pa- tients who received the same operation and identical glucocor- ticoid therapy. Other pituitary functions were not impaired postoperatively. We conclude that (1) the hypercortisolism caused by an ACTH-secreting pituitary microadenoma sup- presses the normal pituitary secretion of ACTH and often that of GH and LH; (2) this suppression persists postoperatively, but gradually resolves in most patients; (3) a normal cortisol re- sponse to ACTH is a good indication that the pituitary-adrenal axis has recovered; (4) there is no evidence of a persisting hy- pothalamic defect after removal of ACTH-secreting microa- denomas; and (5) pituitary microadenomas appear to be the pri- mary cause of Cushing's disease in these patients. (65 Refs)

11. CLINICAL TRIAL OF THE SIZE-REDUCING EFFECT OF BROMOCRIPTINE ON PITUITARY TUMORS.

Wollesen F, Andersen T, Karle A
Endokrinologisk afdeling, Kobenhavns kommunes hospital, DK-2650 Hvidovre, Denmark
Ugeskr Laeger; 143(52):3534-3538 1981

The effect of bromocriptine (BC) treatment on the size re- duction of aggressively growing extrasellar solid pituitary tumors was studied in 20 consecutive patients (8 men and 12 women, 35-76 yr old). Twelve patients were pretreated, mostly by the combination of surgery and radiotherapy; the therapy- free interval of these 12 patients was 5-118 mo. Ten patients received hormone substitution therapy. BC was administered in daily doses of 15 mg (1 patient), 30 mg (12), 60 mg (6) and 160 mg (1) for 2-48 mo. The tumor size was determined by com- puted tomography before and during the BC treatment. The median absolute reduction of the tumor size was 36.5 square mm (mm2) from 94.5 mm2 to 59.5 mm2. The median relative reduction for all 20 patients was by 32%. Three tumors disap- peared completely, 13 were reduced in size by 18-65%, 2 showed growth arrest and two continued to grow during the treatment. Reduction of tumor size or growth arrest occurred in 4/5 patients with normal prolactin secretion. The relative tumor size reduction was significantly and positively correlated with the pretreatment tumor size, but not to the serum levels of hormones, nor to the BC dose, length of treatment, and sex of the patients. The only major side-effect was a reduced need for early morning sleep in 8/20 patients. The immediate suc- cess rate of BC treatment in terms of tumor size reduction was of the same order of magnitude as that of the two conventional therapeutic modalities for large pituitary tumors. (15 Refs) (In DAN)

OTHER THERAPY OF CNS MALIGNANCIES

12. TREATMENT OF CENTRAL NERVOUS SYSTEM TUMORS WITH METHOTREXATE.

Abelson HT, Kufe DW, Skarin AT, Major P, Ensminger W, Beardsley GP, Canellos GP
Sidney Farber Cancer Inst., 44 Binney St., Boston, MA, 02115
Cancer Treat Rep; 65(Suppl1):137-140 1981

Thirteen patients with primary and metastatic CNS tumors have been treated with methotrexate (MTX) using three differ- ent approaches: (a) high-dose MTX with leucovorin (LV) rescue; (b) high-dose MTX with carboxypeptidase (CPDG) rescue; and (c) intraventricular administration of low doses of MTX for extended periods (concentration X time [C X T]). Eleven patients had central nervous system (CNS) lymphoma (1 primary), 1 patient had recurrent medulloblastoma, and an- other patient had metastatic breast carcinoma. All 13 patients received high-dose MTX-LV rescue, while 3 patients were subsequently given MTX-CPDG. One patient received MTX by all three modalities. In patients with CNS lymphomas, com- plete responses (45%) and partial responses (36%) produced CNS disease-free intervals ranging from 1 to 23+ mo. Survival for the complete responders has thus far ranged from 2.5 to 35 mo, while the partial responders survived from 3 to 5 mo. Two patients failed to respond and survived 2.5 and 3 mo. Re- sponses were obtainable with high-dose MTX-CPDG in pa- tients resistant to MTX-LV. One patient who became sensi- tized to CPDG subsequently responded to MTX by intraven- tricular C X T administration. Thus, MTX can be effectively administered to patients with CNS tumors by several different approaches. (Author abstract) (24 Refs)

OTHER CLINICAL ASPECTS OF CNS CANCER

13. BRAIN TUMORS IN THE PEOPLE'S REPUBLIC OF CHINA: A STATISTICAL REVIEW.

Cheng MK

Neurological Service, Massachusetts General Hosp., Boston, MA, 02114

Neurosurgery; 10(1):16-21 1982

A published series of data from Beijing Hsuan Wu Hospital, Shanghai Hua Shan Hospital, and eight other hospitals in seven cities of the People's Republic of China, comprising 12,785 cases of pathologically confirmed brain tumors, are analyzed. Tumors are listed by histological type, location in adults and children, and by sex and age of patients. Summary data are compared with published reports from Western countries and Japan. The rank order of the four most prevalent histological types of tumors, glioma, meningioma, neurinoma, and pituitary adenoma, is the same as in the West, but differs from Japan, where metastatic tumors rank third and neurinomas are fifth. Incidences of vascular, dysembryoplastic, metastatic, and miscellaneous tumors are quite different from either the West or Japan. Of special interest are the very low rate of breast tumor metastasis to the brain (1.3% compared to 7-23% in the West and 11.2% in Japan), and the comparatively high rates of ependymoma (25.3% of all brain tumors) and craniopharyngioma (17.5%) in Beijing Hsuan Wu Hospital in 1979. (19 Refs)

SELECTED PRECLINICAL ASPECTS OF CNS CANCER

14. REGULATION OF PITUITARY GROWTH AND PROLACTIN GENE EXPRESSION BY ESTROGEN.

Lieberman ME, Maurer RA, Claude P, Wiklund J, Wertz N, Gorski J

Dept. Biochemistry and Animal Science, Univ. Wisconsin, Madison, WI, 53706

Adv Exp Med Biol; 138:151-163 1982

The site of estrogen action and the molecular events involved in the regulation of prolactin synthesis were studied using monolayer cultures of dispersed rat pituitary cells. Primary cultures of rat pituitary cells respond to estradiol by increased incorporation of precursors into prolactin. Time and magnitude of response are in agreement with that observed under in vivo conditions suggesting that est rogen exerts its effect through a direct action on the pituitary gland. Chronic treatment with diethylstilbestrol caused sustained proliferation of pituitary tumors in the Fisher 344 rat, but not in the Holtzman rat. (33 Refs)

15. HISTIDYL-PROLINE DIKETOPIPERAZINE SUPPRESSES PROLACTIN SECRETION IN HUMAN PITUITARY TUMOUR CELL CULTURES.

Melmed S, Carlson HE, Hershman JM

Dept. Medicine, Univ. California Los Angeles Sch. Medicine, Los Angeles, CA

Clin Endocrinol (Oxf); 16(1):97-100 1982

Because histidyl-proline diketopiperazine (HPD), a metabolite of TRH, has been shown to suppress prolactin (PRL) release by rat pituitary tumor cells, human pituitary tumor cells were exposed to this compound. Monolayer cell cultures were initiated from pituitary tissue removed by transsphenoidal surgery from two patients with prolactin-secreting microadenomas. Tumor fragments were mechanically dispersed; cells were seeded into multiwell plates and incubated in Ham's F-10 medium enriched with fetal calf serum (20%). HPD (7.5 ng/ml) suppressed PRL release by both tumor cell cultures. Theophylline reversed the inhibition of PRL release induced by HPD. The data raise the possibility that HPD may act as an endogenous prolactin-inhibiting factor in man. (Author abstract) (7 Refs)

16. ESTABLISHMENT OF FUNCTIONAL HUMAN PITUITARY TUMOR CELL CULTURES.

Melmed S, Odenheimer D, Carlson HE, Hershman JM

Endocrine Res. Lab., Medical and Res. Services, Wadsworth Veterans Admin. Medical Center, Los Angeles, CA

In Vitro; 18(1):35-42 1982

Five primary human pituitary tumor cell cultures were initiated from adenoma fragments obtained from patients with prolactin-secreting adenomas and acromegaly. Functional cell cultures were maintained and propagated in monolayer or suspension culture for up to 9 mo. Optimal cell viability and growth were achieved using Ham's F10 medium enriched with 20% fetal bovine serum, although cells from a patient with acromegaly also grew in serum-free, defined, hormone-containing medium. Bromocriptine (100 ng/ml) did not alter the growth curve of replicating cells derived from a patient with acromegaly. These cells initially secreted 5.5 ug human growth hormone/10(6) cells, and hormone production diminished after 6 wk. Prolactin secretion by cells derived from prolactinomas (0.5 to 1.3 ug/10(6) cells/24 hr) was stimulated by thyrotropin-releasing hormone (10 ng/ml) in two of the cultures. Both dopamine (10 ng/ml) and nickel chloride (1 mM) suppressed PRL secretion. These studies demonstrate that responsive human pituitary tumor cell cultures can be initiated and maintained. (Author abstract) (26 Refs)

17. DEVELOPMENT OF A MONOCLONAL ANTIBODY AGAINST A TUMOR-ASSOCIATED ANTIGEN.

Peng WW, Bressler JP, Tiffany-Castiglioni E, De Vellis J

Lab. Nuclear Medicine and Radiation Biology, Univ. California, Los Angeles, CA, 90024

Science; 215(4536):1102-1104 1982

A monoclonal antibody-producing hybrid cell line was obtained by fusing mouse myeloma cells with spleen cells from a mouse immunized with C6 glioma cells. This antibody binds to a specific cell-surface antigen that is present on C6 rat glioma cells, transformed astrocytes and oligodendrocytes, and a human glioma cell line but is absent on a normal glial cell line, fibroblasts, and primary cultures of astrocytes and oligodendrocytes. The antigen also appears on tumor tissue of transformed oligodendrocytes but not on normal brain tissue. (Author abstract) (18 Refs)

18. COMPARATIVE STUDIES ON ANTI-TUMOR EFFECTS OF NITROSOUREAS, ACNU AND MCNU, ON EXPERIMENTAL BRAIN TUMORS.

Harada K, Kiya K, Okamoto H, Uozumi T
Dept. Neurosurgery, Hiroshima Univ., Hiroshima 734, Japan
Neurol Med Chir (Tokyo); 21(10):1017-1023 1981

Comparative anti-tumor effects of ACNU (1-(4-amino-2-methyl-5-pyrimidinyl)methyl-3-(2 chloroethyl)-3 nitrosourea) and MCNU were studied on 20-methylcholanthrene-induced C57 black mouse maligrant gliomas (MG-cells) and rat glial tumors (C6-cells) in vitro and in vivo. The inhibitory effects of ACNU and MCNU in vitro were dependent on dose and time. The concentration showing inhibitory effect was more than 10 ug/ml. ACNU was slightly more effective than MCNU. ACNU significantly inhibited DNA synthesis at concentrations higher than 10 ug/ml, but had no such effect on RNA and protein syntheses. MCNU also inhibited DNA synthesis similar to but less than that of ACNU. By a single intraperitoneal administration on day 5, an increased life span (ILS) was observed with ACNU (120.3% increase) and with MCNU (100.4%). The optimal dose was 25 mg/kg/day for both drugs. The therapeutic ratio, or optimal dose divided by the dose producing an increased life span of 30% over controls, of ACNU was 4.17 and that of MCNU was 6.67. When 25 mg/kg/day of ACNU was administered intraperitoneally on day 5, 2 out of 10 mice survived over 60 days. In case of MCNU, 1 out of 10 mice survived. A single administration of ACNU or MCNU was more effective for the increased life span compared with intermittent administration. From these results, it is suggested that the new water soluble nitrosourea, MCNU, can be utilized as a chemotherapeutic agent against brain tumors as in the case of ACNU. (Author abstract) (28 Refs) (In JPN)

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NEUROGLIAL CELL TUMORS

1. MALIGNANT HEMISPHERIC ASTROCYTOMAS IN THE ADULT. LIMITS OF THE SCANNER.

Caille JM, Guibert-Tranier F
Service de Neuroradiologie, Hopital Pellegrin-Tripode, F 33076 Bordeaux, France
Neurochirurgie; 27(5):261-267 1981

The diagnostic accuracy of computed axial tomography (CAT) in malignant hemispheric astrocytomas is calculated based on four studies involving 920 patients. The detection of gliomas by CAT scanner was above 95% in all series. In many cases, results of the CAT scan indicated an anomaly but did not suggest a precise diagnosis or suggested several possible diagnoses. False positives results ranged from 5-15% in four studies. Diagnostic errors most frequently occurred with metastases, with benign lesions such as meningiomas, abscesses, in-

HE 20. 3173/2:

flammatory lesions, and vascular malformations. True positives results were achieved in about 70% of the diagnostic tests. The opacification of the tumor for CAT investigation depended on two factors: the vascular pool and the diffusion of the contrast medium from the intravascular space toward the extracellular space. Tumor vol could not be precisely defined by CAT investigation. In order to characterize lesions identified by CAT scanners, angiography was recommended as a means of clarifying diagnostic ambiguities. (31 Refs) (In FRE)

2. THE ROLE OF STEREOTACTIC BIOPSY IN THE THERAPEUTIC APPROACH TO MALIGNANT GLIOMAS.

Sedan R, Peragut JC, Farnarier P, Hassoun J, Torres T
Service de Neurochirurgie fonctionnelle, C.H.R. de la Timone, boulevard Jean-Moulin, F 13005 Marseille, France
Neurochirurgie; 27(5):285-286 1981

Three series of stereotactic biopsies of intracerebral tumors were performed using prebiopsy angiography. A total of 770 biopsies were analyzed. Inconsequential bleeding occurred in approx 30% of the biopsies. Bleeding accompanied by a hematoma occurred in 0.25% of the biopsies. A transitory deficit occurred in 3.8% of the patients. Transitory meningitis was induced in 0.25% of the patients. There were serious, long-term consequences (hemiplegia) in 1.4% of the cases, and nine deaths occurred. In 7.5% of the cases, the lesion was missed or there was an error in the interpretation of the biopsy results. In 41.5% of the cases, the prebiopsy diagnosis which was uncertain or incomplete was clarified. [illegible] 28% of the cases, the prebiopsy diagnosis was fundamentally altered. In almost 75% of the cases, the tumors were situated in areas which were problematic either because of the depth of the lesion or because of the functional involvement of the area. Stereotactic biopsies are recommended for intracerebral tumors because they provide important preoperative information on the tumor type and possible extent and characteristics of the tumor. (no Refs) (In FRE)

3. MALIGNANT GLIAL TUMORS. DIFFICULTIES ENCOUNTERED IN HISTOPATHOLOGICAL DIAGNOSIS.

Hauw JJ, Poisson M, Escourolle R
Laboratoire de Neuropathologie Charles Foix, Hopital de la Salpetriere, 47, boulevard de l'Hopital, F 75651 Paris, France
Neurochirurgie; 27(5):269-271 1981

The diagnosis of malignant glial tumors at the first surgical intervention can be established on the basis of classic glial cell tests, or by the presence of glial fibrillary acidic (GFA) protein. Immunoperoxidase techniques are used to determine the presence of GFA which indicates the astrocyte characteristics of a tumor. Two problems limit this diagnostic test. Necrotic zones and immature or undifferentiated cells of malignant gliomas contain little or no GFA. Hypertrophied glial cells are rich in GFA. The degree of malignancy of glial tumors is often extremely difficult to determine. Tumors should be carefully studied with detailed attention to their histological characteristics so that they can be graded (I- IV) and prognoses can be established. A benign astrocytoma (Grade I-II) must be distinguished from a glioblastoma or an anaplastic astrocytoma (Grade IV or III). Hypercellularity is a poor prognostic factor. The presence of giant cells in the glial tumor is a favorable element. The diagnosis of recurrent tumor following treatment can lead to additional difficulties. Radionecrosis, glial proliferation in postsurgical scars, and astrocyte gliosis induced by radiotherapy or chemotherapy have all been associated with therapy for glial tumors. (13 Refs) (In FRE)

4. INTRA-ARTERIAL CHEMOTHERAPY FOLLOWING BLOOD-BRAIN BARRIER DISRUPTION IN A PATIENT WITH MALIGNANT GLIOMA.

Hill SA, Newelt EA
Div. Neurological Surgery, Oregon Health Sciences Univ., 3181 S.W. Sam Jackson Park Road, Portland, OR, 97201
J Neurosurg Nurs; 14(2):94-97 1982

In dogs, a brief (20-30 sec) intracarotid infusion of a hypertonic 25% mannitol soln, followed by an intracarotid infusion of methotrexate (MTX), led to the uptake of a high level of MTX by the brain tissue. Enhanced computed tomography (CAT) scans confirmed the disruption of the blood-brain barrier (BBB) on the infused side. Experiments using adriamycin and cis-diamminedichloroplatinum(II) are now in progress. Osmotic BBB disruption by intracarotid mannitol infusion was performed in nine patients with histologically confirmed brain tumors (metastatic tumors or Grade III-IV astrocytomas). These patients were given 35 intracarotid infusions of MTX after the mannitol infusions. Enhanced CAT scans confirmed BBB disruption on the infused side. No conclusions could be drawn regarding the efficacy of this treatment, but the results of this Phase I clinical trial provided evidence that BBB disruption is a relatively nontoxic means of increasing drug delivery to both the tumor and the surrounding tissues. One of these patients, a 55-yr-old woman with a frontal lobe glioblastoma multiforme, received five courses of MTX (100 mg each) after osmotic BBB disruption, beginning shortly after a course of postoperative radiotherapy (5,000 rads). Repeat CAT scans disclosed slight tumor regression, but the patient declined further treatment when the symptoms progressed, after 4 mo of chemotherapy. (8 Refs)

5. THE BIOLOGICAL BASIS OF THERAPEUTIC STRATEGIES IN MALIGNANT GLIOMAS. GENERAL ONCOLOGICAL DATA, CURRENT METHODS AND RESULTS, PROSPECTS.

Chatel M, Menault F
Service de Neurologie, Laboratoire de Neuropathologie, Centre Hospitalier Universitaire, F 35033 Rennes, France
Neurochirurgie; 27(5):299-303 1981

Studies on current therapeutic methods for malignant gliomas are reviewed. Surgery is considered primary treatment for reducing the tumor mass and suppressing edematous and necrotic zones. Radiotherapy is more limited in its use but its effectiveness has been well documented. Factors which influence the failure of chemotherapeutic treatment of gliomas include the small number of effective drugs, the poor use of drugs, the absence of correlation between cellular kinetics and drug use, and the cellular heterogeneity of malignant gliomas. Currently only three experimental methods exist for analyzing drug and tumor interactions. These methods include tests on formations of cellular colonies, chemosensibility tests, and subcutaneous or intracerebral implantations in mice. Chemotherapeutic treatment of malignant gliomas has had very modest results. Chemotherapy has prolonged recurrence free rates and has improved the quality of life during survival. These results have been overshadowed by the constraints which the treatment places on patients and by the constant escape of the tumors from chemotherapeutic control. (28 Refs) (In FRE)

6. CURRENT EXPERIENCE WITH STEREOTACTIC IRRADIATIONS IN THE TREATMENT OF HEMISPHERIC GLIOMAS.

Szikla G, Betti O, Szenthe L, Schlienger M
Service de Neurochirurgie B, Centre Hospitalier Sainte-Anne, 1, rue Cabanis, F 75014 Paris, France
Neurochirurgie; 27(5):295-298 1981

Implanted or injected stereotactic irradiation was used in the treatment of 11 malignant gliomas, 28 astrocytomas, and 17 recurrent, low grade gliomas. The mean survival of the patients with malignant gliomas was 12.7 mo, and all patients died. Irradiation treatment for malignant gliomas is recommended because of good tolerance of the treatment. The apparent stabilization for good clinical cases lasted an av 10 mo with subsequent rapid deterioration. Three patients with astrocytomas died 4, 8, and 13 mo after irradiation. There were no clinical or radiographic signs of tumor growth in 19 cases. Functional deficits occurred in four patients, and six patients (21%) showed signs of recurrence after an av remission period of 2 yr without functional loss during that time. Irradiation therapy was associated with the disappearance or diminution of epileptic seizures in several patients in this group. The secretions of the cystic wall were stopped in 15/17 patients receiving injected irradiation. In three patients retreatment was necessary at 1, 2, and 4.5 yr following the original therapy. Immediate surgical risks and late functional loss were low in all groups tested. (10 Refs) (In FRE)

7. THE ROLE OF SURGERY IN THE TREATMENT OF SUPRATENTORIAL MALIGNANT GLIOMAS.

Pecker J, Scarabin JM, Dekkiche M, Allaire C
Service de Neurochirurgie, C.H.U. Rennes, 1, rue H. Le Guillou, F 35000 Rennes, France
Neurochirurgie; 27(5):287-293 1981

The literature is reviewed for survival rates following surgery and surgery asso ciated with radiotherapy and chemotherapy for malignant gliomas. Operative mortality has improved decreasing from 25% to 5% in the last 10 yr. Mean overall survival calculated from all series is about 10 mo. Surgery alone has provided a mean survival of 5-6 mo with a mean survival of 22.7% at 12 mo. Surgery followed by radiotherapy has provided mean survival rates of 7.4 mo with partial excision and radiation therapy and 10.33 with wide excision and radiation therapy. Surgery (partial excision) and radiotherapy has led to a 30.7% survival rate at 12 mo. The decrease in operative mortality is attributed to improved surgical and anesthetic techniques, to better surgical control of intracranial hypertension, and to better assessments of the tumor extent and vol from computed axial tomography. Because of the short mean survival times and the functional impairments associated with surgery, careful selection of operative cases is recommended, and radiotherapy is advised as adjunctive therapy for the treatment of malignant gliomas. (54 Refs) (In FRE)

8. THE PRINCIPAL FIELDS OF RESEARCH INTO THE PATHOGENESIS OF GLIOMAS.

Cohadon F
Laboratoire de Neurochirurgie Experimentale et Neurobiologie, Groupe Hospitalier Pellegrin, place Amelie-Raba-Leon, F 33000 Bordeaux, France
Neurochirurgie; 27(5):241-245 1981

Experimental models studying the pathogenesis of gliomas are focused on chemically or viral induced tumors in animals. The transplacental injection of ethyl-nitrosourea in rats has produced a high rate (80-100%) of cerebral tumors of mixed types in the offspring. Repeated injections of methyl-nitrosourea in the adult rat has produced more homogenous cerebral tumors (glioblastomas most often) in 60-70% of the rats. Viral induced tumors have been produced in dogs inoculated at birth with intracerebral injections of Rous sarcoma virus. Glioma promotion is considered a result of the failure of a hypothetical immune mechanism of surveillance. The absence of systemic metastases of the gliomas is an indirect but convincing proof in favor of a surveillance immune system which eliminates the malignant cells when they leave the immunological protection of the brain. This theory is further supported by the clear immunosuppression of some patients with gliomas. At the present time, there is not definite identification of initiation or promotion factors in the pathogenesis of human gliomas. (7 Refs) (In FRE)

9. BRAIN STEM GLIOMAS: AN AUTOPSY STUDY OF 25 CASES.

Mantravadi RV, Phatak R, Bellur S, Liebner EJ, Haas R
Dept. Radiology, Univ. Illinois Hosp., P.O. Box 6998, Chicago, IL, 60608
Cancer; 49(6):1294-1296 1982

The study analyzed the extent of tumor at autopsy in 25 patients with a brainstem glioma. Primary tumor in the pons comprised the majority of cases, followed by medulla and midbrain. Hist ologically, 48% of the tumors were glioblastoma multiforme. The tumor spread was found to be dependent on the site of origin and the grade. Pontine tumors involved the adjacent structures more extensively than the tumors of midbrain and medulla. Contiguous cephalad and caudad involvement was frequent with Grade III and Grade IV tumors. The extent of meningeal involvement was limited to those surrounding the main tumor mass. It is concluded that in the treatment of brainstem gliomas, irradiation through fields limited to the brainstem, adjoining temporal lobes, cerebellum, and proximal spinal cord would be adequate. (Author abstract) (11 Refs)

10. THE DIAGNOSIS AND THERAPEUTIC MANAGEMENT OF MALIGNANT GLIOMAS.

Rougier A, Pigneux J, Richaud P, Cohadon F
Service de Neurochirurgie A, Hopital Pellegrie, F 33000 Bordeaux, France
Neurochirurgie; 27(5):315-320 1981

In a series of 111 space-occupying lesions assumed to be malignant gliomas on the basis of clinical and scanner findings, the diagnosis was corrected in 11 cases by biopsy and in one case by surgical findings. In 45/98 confirmed cases of malignant glioma, a macroscopically complete surgical resection was performed. Fifteen cases were treated with interstitial irradiation, and seven cases with intracystic injection of radiation. In 27 cases, conventional and stereotactic therapy was not possible, and combination radiotherapy-chemotherapy was proposed. A decision to deliver no therapy was made in three cases. of those patients with active astrocytomas treated with surgery and radiotherapy, 50% were alive at 34 mo compared to a 12 mo 50% survival rate for those patients treated with radiotherapy alone or in association with chemotherapy. Of those patients with polymorphous glioblastomas treated with surgery and radiotherapy, 50% were alive at 15 mo compared to a 4 mo 50% survival rate for those patients treated with radiotherapy alone or in association with chemotherapy. Considering the rapid rate of deterioration for those patients with inoperable tumors, a purely palliative therapeutic approach is recommended in place of the radiotherapy and chemotherapy that was delivered in this series. (16 Refs) (In FRE)

MESODERMAL TUMORS OF THE CNS

11. CLINICAL AND PATHOLOGICAL STUDY OF MENINGIOMAS OF THE FIRST TWO DECADES OF LIFE.

Deen HG, Scheithauer BW, Ebersold MJ
Dept. Neurologic Surgery, Mayo Medical Sch., Rochester, MN, 55905
J Neurosurg; 56(3):317-322 1982

The clinical features and pathological materials of 51 cases of histologically verified meningiomas in patients under 21 yr of age were reviewed. The age range was 7 to 20 yr, with the majority of cases being clustered in the second decade of life. There was virtually a 1:1 sex ratio, with 26 females and 25 males. Thirty-eight patients had intracranial meningiomas, 3 had intraorbital tumors, and 10 had intraspinal tumors. Twelve patients (24%) had neurofibromatosis. Twenty patients (39%) had tumor recurrence. The cases were subdivided into five histological categories: meningotheliomatous, fibrous, transitional, psammomatous, and papillary. In each case, the clinical course was correlated with histological subtype. The 15-yr survival rate in patients with intracranial meningiomas of all types was 68%. Factors adversely affecting survival included infratentorial location, papillary histology, and evidence of brain invasion. (Author abstract) (23 Refs)

12. ROLE OF RADIATION THERAPY IN THE MANAGEMENT OF MENINGIOMA.

Carella RJ, Ransohoff J, Newall J, Salcman M, Matsui T
Dept. Radiation Oncology, New York Univ. Medical Center, 500 First Ave., New York, NY, 10016
Neurosurgery; 10(3):332-339 1982

Radiation therapy (RT) of 68 patients (49 females, 19 males; 25-80 yr old) with meningiomas is reviewed. Surgery followed by RT was treatment of 43 patients, 42 with known residual tumor and 1 with a malignant meningioma thought to be totally removed. RT was used for 14 patients with recurrence following surgery: combined with surgery in 11 and alone in 3. RT as primary treatment was used in 11 patients without pathological confirmation of tumor. The most common tumor locations were the parasagittal region, on the cerebral convexities, and on the sphenoidal ridge. The usual tumor dose was 5,500-6,000 rad in 6-6.5 wk (range 5,000-7,7000 rad with one patient initially receiving 6,000 rad followed by 4,000 rad for recurrence). Of the 43 patients treated with surgery and postoperative RT, 41 survived and 2 died during follow-up periods of 1-10 yr. All these patients maintained their best neurological classifications. Of the 14 patients treated with RT for recurrence, 5 patients showed improved neurological function, 2 remained unchanged, and 7 deteriorated; 5 patients died of tumor 1-3 yr following treatment. All 11 patients treated with RT alone as initial therapy survived for 3-6 yr; 9 showed neurological improvement and 2 remained stable. Of 11 patients with malignant meningiomas, 3 died of disease. Four case reports are presented illustrating clinical, pathological, and radiological responses. Recommendations are made for use of RT in treatment of meningioma. (12 Refs)

TUMORS OF THE CRANIAL AND SPINAL NERVE ROOTS

13. CELLULAR SCHWANNOMA. A VARIETY OF SCHWANNOMA SOMETIMES MISTAKEN FOR A MALIGNANT TUMOR.

Woodruff JM, Susin M, Godwin TA, Martini N, Erlandson RA
Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
Am J Surg Pathol; 5(8):733-744 1981

Peripheral nerve tumors from 14 patients (7 men, 7 women, 25-81 yr old) were histologically identified as cellular schwannomas. The most common sites of origin were the posterior mediast inum (4/14), pelvis (3/14), and neck (2/14). The nerve of origin was identified in only 3/14 patients. Due to a variety of confusing histologic features (including moderate mitotic activity and moderate nuclear atypia), 6/14 tumors had been classified as fibrous histiocytoma, leiomyoma, malignant peripheral nerve sheath tumor, or sarcoma of uncertain origin. The erroneous impression of a malignancy was reinforced in two patients by clinical evidence of bony erosion and destruction. However, follow-up data on 8/14 patients and the presence of one tumor for 20 yr before excision indicated this tumor to be benign. (6 Refs)

14. THE MALIGNANT SCHWANNOMA.

Nagel K, Ghussen F
Chirurgische Universitatsklinik, Joseph-Stelzmann-Strasse 9, D-5000 Koln 41, W. Germany
Med Klin; 77(2):45-47 1982

Malignant schwannoma (MS) is reviewed. MS is a rare neoplasm of the neural sheath, accounting for 2-12% of all neurofibromas or schwannomas. MS occurs with equal frequency in both sexes. The extremities are most commonly affected. MS is most often diagnosed in later stages. Symptoms include motor or sensory disturbances and general tumor-related compression symptoms. Advanced MS may be accompanied by abnormal laboratory findings. Diagnosis of symptoms is difficult, because no MS-specific symptoms are known. MS is frequently associated with von Recklinghausen's neurofibromatosis. It is uncertain whether MS can develop from benign schwannoma. The primary histological characteristic of MS is the presence of spindle-shaped cells showing cellular and nuclear polymorphism, a high proportion of mitotic cells, and frequently a small amount of cytoplasm. Tumor tissue contains bundles of fibers that stain with collagen- and silver-stains. MS originates from Schwann cells and may form mesectodermal or mesodermal structures. Treatment of choice is wide excision. Amputation is recommended as the safest method for MS of the extremities. In one series of patients survival time ranged from several mo to greater than 10 yr (av 1.4 yr). MS may metastasize to the lungs, liver, bones, or brain. Metastasis is usually hematogenic, although lymphatic metastasis has been reported. Results of radiotherapy, combination therapy, and monochemotherapy have not been satisfactory. (23 Refs) (In GER)

SECONDARY TUMORS OF THE CNS

15. STRUCTURAL CHANGES IN HUMAN PITUITARY TUMOR AFTER BROMOCRIPTINE THERAPY.

Rengachary SS, Tomita T, Jefferies BF, Watanabe I, VanGilder JC, Carmel PW
Neurosurgery Section, Veterans Admin. Medical Center, 4801 Linwood Blvd., Kansas City, MO, 64128
Neurosurgery; 10(2):242-251 1982

The case of a 54-yr-old man with an invasive prolactinoma who was treated with bromocriptine (BRO: 1.25 mg 3x/day with gradual increment to 15 mg 3x/day over a period of 2 wk, then 15 mg/day for 4 wk) is presented. Light and electron microscopic changes of different parts of the tumor before and after BRO were examined. A similar study was performed after BRO therapy on a growth hormone-producing tumor in a 52-yr-old man with acromegaly. In the patient with a prolactinoma the tumor was subtotally excised after 6 wk of BRO therapy and the patient subsequently received 4,500 rad radiotherapy in 4 wk; light microscopy demonstrated that after BRO treatment the neoplastic cells had shrunken uniformly in size and contained small, condensed pyknotic nuclei and scanty cytoplasm. Immunoperoxidase revealed weak cytoplasmic staining for prolactin in approx half of the cells. Electron microscopy demonstrated that after BRO treatment the av size of the cells was markedly reduced, with the reduction in cytoplasm disproportionately large compared with that of the nucleus. Loss of ribosomes, rough endoplasmic reticulum, and Golgi complexes, and an apparent increase in the number of endocrine granules within the cytoplasm, were noted. More lysosomal crinophagic structures were seen. BRO decreased the total cell area to about 40% of original size and increased the mean granule count per cell from 25 to 85. No such changes were observed in the growth-hormone-producing tumor. For large and invasive pituitary adenomas, treatment with BRO may be superior to surgery and have fewer complications. (60 Refs)

16. SIZE REDUCTION OF EXTRASELLAR PITUITARY TUMORS DURING BROMOCRIPTINE TREATMENT: QUANTITATION OF EFFECT ON DIFFERENT TYPES OF TUMORS.

Wollesen F, Andersen T, Karle A
Div. Endocrinology, Hvidovre Hosp., 2650 Hvidovre, Denmark
Ann Intern Med; 96(3):281-286 1982

The well-known size-reducing effect of bromocriptine on prolactinomas was tested on five types of large, extrasellar pituitary tumors. Twenty patients were treated prospectively for up to 4.5 years with bromocriptine, 30 or 60 mg/day (2 patients received 15 mg and 160 mg, respectively). The effect on the size of the pituitary tumors was quantitated by planimetry of computed tomographic scans before and during treatment. The immediate success rate was 16 of 20 tumors. Eleven nonsecreting tumors were reduced by a median of 32% (range of reduction for 50% of cases, 18%-41%) with an immediate success rate of 9 of 11. Nine secreting tumors (4 that secreted prolactin; 3, growth hormone; 1, adrenocorticotropic hormone; and 1, thyroid stimulating hormone) were reduced by a median of 51% (range of reduction for 50% of cases, 25%-72%). The reduction in tumor size was significantly associated with pretreatment size (r = 0.6360, p less than 0.005), but not with the serum concentration of any hormones assayed or previous radiation treatment. Bromocriptine causes a clinically significant reduction in size of nonsecreting as well as secreting pituitary tumors with the same success rate as that of conventional treatments. (Author abstract) (35 Refs)

OTHER THERAPY OF CNS MALIGNANCIES

17. A NEW TREATMENT OF MALIGNANT BRAIN TUMOR -1: LOCAL INJECTION OF BLEOMYCIN.

Nakazawa S, Ohwaki K, Shimura T, Itoh Y, Yajima K
Dept. Neurosurgery, Nippon Medical Sch., Tokyo, Japan
No Shinkei Geka; 9(13):1487-1493 1981

This is a paper about a new trial of treatment for malignant brain tumor by local injection of bleomycin (BLM). The new method of intraneoplastic BLM injection is as follows; in the cases with subtotal or partial removal of the tumor, Ommaya's device was retained in the tumor bed, and its reservoir was fixed sc on the skull. BLM was injected by sc puncture into the reservoir every other day. Usual total dose of BLM was 30-80 mg. The patients were usually treated with 60Co-irradiation and immunotherapy after local injection of BLM. Twelve patients with malignant brain tumor were treated by the above mentioned method and a follow-up study was done. The 1 yr survival rate was 50% and 3 yr survival rate was 25%. Each case of primary sarcoma, medulloblastoma and malignant oligodendroglioma survived for a very long time. However, most of the patients especially those with glioblastoma died of recurrence in about 1 yr or so in spite of temporary improvement of their clinical symptoms and clinical findings. The scintillation scanning of BLM labeled 57Co was utilized to make clearance curves of the drugs in the patients with malignant brain tumor. From the results, it could be presumed that locally injected BLM remained in the tumor tissues for a longer time and killed malignant tumor cells completely. However, an unfavorable fact was that locally injected BLM was retained within the tumor tissue less than 2-3 cm apart from the cavity, showing no efficacy to prevent tumor proliferation in more remote areas. In conclusion, the local injection of BLM seems to be very effective for the treatment of malignant brain tumors if it is used together with iv or ia injection of other chemotherapeutic drugs. (19 Refs) (In JPN)

18. A PHASE I STUDY OF INTRACAROTID ARTERY INFUSION OF CIS-DIAMMINEDICHLOROPLATINUM(II) IN PATIENTS WITH RECURRENT MALIGNANT INTRACEREBRAL TUMORS.

Stewart DJ, Wallace S, Feun L, Leavens M, Young SE, Handel S, Mavligit G, Benjamin RS
Ontario Cancer Foundation Clinic, Ottawa General Hosp., 501 Smyth Road, Ottawa, Ontario K1G 8L6, Canada
Cancer Res; 42(5):2059-2062 1982

A Phase I study of intracarotid cis-diamminedichloroplatinum was performed in 11 patients with intracerebral tumors (5 glioblastoma, 4 melanoma, 1 meningeal sarcoma, and 1 lung carcinoma) progressing after radiation +- chemotherapy. The internal carotid artery was temporarily cannulated by a percutaneous transfemoral approach. All patients received iv heparin, mannitol, and fluids; seven received dexametha sone, 50 mg iv, twice the day before and the day of treatment. Intracarotid cis-diamminedichloroplatinum, 60-100 mg/sq m in 175 to 250 ml 45% NaCl solution with 1,000 units heparin, was infused over 1 hr. Six patients received two or more courses (maximum of 6) at 2-to 8-wk intervals. Gastrointestinal toxicity was mild to moderate. Ototoxicity was minor. Central nervous system (CNS) toxicity was focal, severe, permanent, and possibly due to embolus in one patient at 75 mg/sq m; focal and reversible in one patient at 100 mg/sq m; and generalized but reversible in one patient at 75 mg/sq m. Possible CNS toxicity was noted in two additional patients. Two patients with CNS toxicity developed permanent ipsilateral retinal toxicity, and one patient without CNS toxicity developed bilateral decreased visual and auditory acuity 2 wk after his sixth treatment. Renal and hematological toxicity and orbital pain were mild. Response status included: early death, one; probable responses, six (2+, 4+, 6, 6+, 8, and 8+ mo); stabilization, two (3+ and 4 mo); and failure, two. We recommend cis-diamminedichloroplatinum (60 mg/sq m) every 2-4 wk for Phase II studies. Severe CNS and retinal toxicity are possible. (Author abstract) (14 Refs)

19. INTRACEREBRAL CHEMOTHERAPY: CHRONIC MICROINFUSION OF CISPLATIN.

Kroin JS, Penn RD, Sklar F, Neuwelt EA
Dept. Neurosurgery, Rush Medical Coll., 1753 West Congress Parkway, Chicago, IL, 60612
Neurosurgery; 10(3):349-354 1982

Chronic intracerebral microperfusion of cisplatin into the extracellular space of the brain of normal Wistar rats was investigated. Small stainless steel cannulas were connected to osmotic minipumps and stereotactically placed into the midline cerebellum or frontal cortex. Cisplatin was pumped into the brain at a rate of 0.9 ug/hr for periods up to 1 wk. Brain tissue was analyzed for total platinum content at 1-mm intervals from the cannula tip. In three rats in which cisplatin was infused for 150-160 hr, the amount of drug remaining ranged between 26 and 26.8% of the estimated amount of drug pumped. In a fourth rat with infusion for 100 hr, the amount of drug remaining was 27.4%. At 5 mm from the injection source the platinum concentration was greater than 2 nanog/mg of tissue wet wt in either direction. Concentrations were considerable near the cannula. When pieces of brain at greater distances from the cannula site were analyzed, no detectable platinum was observed. In comparison, no detectable levels of platinum were found in the brain 2 hr after iv injection of cisplatin (5 mg/kg), while plasma levels were near 1 ug/ml at the time of death. It is estimated that one cannula would be sufficient to treat a 1-cm tumor or a larger tumor that could be surgically reduced. A multiple cannula system would be appropriate for inoperable tumors up to 2 cm in diameter. For larger tumors, this system would not produce high enough drug levels. Microperfusion can be used to attain adequate and sustained drug levels over a considerable region of tissues without the problems of systemic toxicity. (39 Refs)

20. ASSESSMENT OF THE LONG-TERM EFFECTS OF PRIMARY RADIATION THERAPY FOR BRAIN TUMORS IN CHILDREN.

Danoff BF, Cowchock S, Marquette C, Mulgrew L, Kramer S
Dept. Radiation Therapy and Nuclear Medicine, Hosp. Univ. Pennsylvania, Philadelphia, PA, 19104
Cancer; 49(8):1580-1586 1982

One-hundred-twelve children with primary brain tumors received definitive radiotherapy between the yr 1958-1979. Sixty-nine patients were alive at intervals of 1-21 yr. Thirty-eight patients underwent neurologic and endocrine evaluation, psychologic and intelligence testing, and assessment for second malignancy post-treatment. A second intracranial malignancy developed in one child, for an incidence of 1.6%. Performance status was good to excellent in 89% of the patients studied. Seventeen percent of the group were mentally retarded. Behavioral disorders were identified in 39% of the patients, 59% of the mothers, and 43% of the fathers. Of the 23 patients with nonparasellar tumors, 6 were found to have growth hormone deficiency, including 2 patients with panhypopituitarism. Disability was related to age under 3 yr at the time of treatment and tumor extension to the hypothalamus. (Author abstract) (33 Refs)

21. COMBINED MODALITY APPROACH FOR BRAIN TUMORS.

Shapiro WR
George C. Cotzias Lab. Neuro-Oncology, Memorial Sloan-Kettering Cancer Center, New York, NY, 10021
Cancer- Achievements, Challenges, and Prospects for the 1980s, Proceedings of an International Conference held in New York, 14-16 September, 1980. Vol. 2, Memoriel Sloan-Kettering Cancer Center New York, NY. Burchenal, J. H. and Oettgen, H. F., eds. (New York, Grune and Stratton), 944 pp., 1981.

Multimodality therapy studies concerning such primary brain tumors as glioblastoma multiforme and malignant astrocytoma (grades III and IV) are reviewed. Surgery, radiotherapy, chemotherapy, radiosensitizers, in vitro and animal model testing of drugs for human brain tumor chemotherapy, and the role of the blood-brain barrier in chemotherapy are discussed. Randomized prospective protocols have demonstrated the definite but modest effectiveness of nitrosoureas. Combination chemotherapy appears more effective than single drug treatment. (30 Refs)

22. BRAIN TUMORS.

Shapiro WR
Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
Cancer Chemotherapy 1981- The EORTC Cancer Chemotherapy Annual 3. Pinedo HM, ed. Amsterdam, Excerpta Medica, 504 pp. 1981.

Major studies on the treatment of brain tumors are reviewed. Treatment of malignant gliomas, childhood brain tumors, and metastatic tumors of the CNS is discussed. Toxicity of chemotherapy and research topics in chemotherapy of CNS tumor are described. The blood-brain barrier and pharmacokinetics of chemotherapeutic agents, animal studies, and tissue culture studies are reviewed. (59 Refs)

OTHER CLINICAL ASPECTS OF CNS CANCER

23. STEREOELECTROENCEPHALOGRAPHY IN CEREBRAL TUMORS.

Rougier A, Sajeaux JC, Certain O, Cohadon F
Service Neuro-Chirurgie A, Hopital Pellegrin, F-33076 Bordeaux Cedex, France
Appl Neurophysiol; 45(4/5):413-418 1982

Stereotactic electroencephalography (SEEG) was performed as an adjunct to other neuroradiographic techniques in 83 patients with suspected brain tumors. The electrical behavior of the tumors and the surrounding cerebral tissues usually differed to an extent that permitted the accurate delineation of the tumor. Malignancies were found on subsequent biopsy in 73/83 patients. Two negative biopsies were associated with small, low-density masses (possibly astrocytomas) of the white matter. Fast Fourier transformation analysis of the SEEG data on these patients might have improved results; the process corrected localization errors in five other patients. The use of SEEG in exploration of expansive intracerebral masses can confirm and enhance the accuracy of tomography and other radiographic techniques, reduce the need for biopsies, and accurately outline areas suitable for interstitial radiation. (9 Refs)

24. STATISTICAL ANALYSIS OF CENTRAL NERVOUS SYSTEM TUMORS IN CHINA.

Huang WQ, Zheng SJ, Tian QS, Huang JQ, Li YX, Xu QZ, Liu ZJ, Zhang WC
(c/o A. Earl Walker) Div. Neurological Surgery, Univ. New Mexico, Sch. Medicine, Albuquerque, NM, 87131
J Neurosurg; 56(4):555-564 1982

The authors present a statistical survey of the general incidence, age distribution, and preferential sites of 25,122 tumors of the central nervous system (CNS), from 12 centers in China. Of these tumors, 22,457 were intracranial and the rest intraspinal. Of the 22,457 intracranial neoplasms collected, tumors of neuroepithelial tissue comprised 43.85%, meningiomas 16.58%, tumors of nerve sheath cells 9.5%, pituitary adenoma 9.52%, congenital tumors 8.46%, secondary tumors 6.8%, vascular malformations and tumors 3.82%, and primary sarcomas 0.72%. Neuroepithelial and meningeal tumors occurred first and second in all series, but the other tumors varied in frequency. There was a higher incidence of nerve-sheath tumors in southern than in northern regions. The age distribution of Chinese patients with tumors of the CNS was lower than that of Caucasians: nearly two-thirds (64.57%) had the clinical onset of their tumor between the ages of 31 and 40 yr, with the peak incidence at 35 yr. Nearly 20% of tumors of the CNS occurred before 20 yr of age. The male;female ratio was 1.53:1; the only tumor with a definite preponderance of females over males was the meningioma. Intraspinal tumors derived from nerve sheaths comprised 47.13% of all tumors within the spinal canal. Meningiomas were second with an incidence of 14.06%, then followed congenital tumors (12.06%) and neoplasms of neuroepithelial tissue (10.83%). Secondary tumors, vascular malformations and neoplasms, and sarcoma were next in order to frequency with 4.6%, 4.5%, and 4.16%, respectively. (Author abstract) (50 Refs)

SELECTED PRECLINICAL ASPECTS OF CNS CANCER

25. COMBINED MODALITY TREATMENT USING RADIATION AND/OR CHEMOTHERAPY IN AN ATHYMIC NUDE MOUSE-HUMAN MEDULLOBLASTOMA AND GLIOBLASTOMA XENOGRAFT MODEL.

Slagel DE, Feola J, Houchens DP, Ovejera AA
Dept. Surgery, Div. Neurosurgery, Univ. Kentucky, Lexington, KY, 40536
Cancer Res; 42(3):812-816 1982

A human medulloblastoma (BN-2) and a glioblastoma (BN-3) were used to determine the effect of combined modality therapy with gamma-radiation, and three chemotherapeutic agents, procarbazine, 1,4-cyclohexadiene-1,4-dicarbamic acid,2,5-bis(1-aziridinyl)3,6-dioxo diethylester (AZQ), and 1,3-bis(2-chloroethyl)-1-nitrosourea (BCNU). The tumor cells were grown in tissue culture and implanted intracranially in the right cerebral hemisphere of NIH Swiss nude mice to a depth of 3 mm. Procarbazine and AZQ were injected ip every 5 days for three treatments. BCNU was injected one time for a single treatment. Radiation was localized to the head. A 60Co unit was used for irradiation at the rate of 125 rads/min 3 days after tumor implantation. Ten experiments were performed using six to nine mice per group and different drug-radiation dose combinations. The day of death was recorded for each animal, and the mean of each treatment group was used to calculate the percentage increase in life span (ILS) compared to the untreated control group. Chemotherapy alone produced a minimal effect, while radiation alone produced minimal effects at 320 to 640 rads with progressively positive effects at 800 and 1,050 rads. When the combination treatment of the human medulloblastoma xenograft with procarbazine was used, the ILS was significantly increased in all four experiments, ranging from 25 to 41%, and was superior to single-modality treatment in all but the 1,050-rad treatment, where it showed an equal effect. The combination treatment using AZQ and BCNU showed no ILS for the medulloblastoma tumor. Combination treatment of the human glioblastoma xenograft using BCNU produced significant ILSs of 105 and 119% and was superior to single-modality treatment with a drug dose of 10 mg/kg and radiation doses of 540 and 800 rads, respectively. The nude mouse-human tumor xenograft model was found to be useful for combined modality studies and should give valuable information for the experimental design of pilot Phase III clinical studies against a variety of brain tumors. (23 Refs)

26. SELECTIVE TOXICITY OF 6-HYDROXYDOPAMINE AND ASCORBATE FOR HUMAN NEUROBLASTOMA IN VITRO: A MODEL FOR CLEARING MARROW PRIOR TO AUTOLOGOUS TRANSPLANT.

Reynolds CP, Reynolds DA, Frenkel EP, Smith RG
(c/o Smith) Cancer Center, Univ. Texas Health Science Center, 5323 Harry Hines Blvd., Dallas, TX, 75235
Cancer Res; 42(4):1331-1336 1982

The compound 6-Hydroxydopamine (6-OHDA) is a neurotoxin for catecholaminergic neurons and neuroblasts. Since frequent marrow involvement in neuroblastoma restricts the exploitation of stored autologous bone marrow for rescue post-chemotherapy, the potential for tumor-specific in vitro toxicity of 6-OHDA was studied. The cytotoxic effect of 6-OHDA on 12 human neuroblastoma cell lines was compared to the effect on nonneuroblastoma cell lines. Most neuroblastoma cell lines were very sensitive to 6-OHDA (av concentration killing 50% of cells, 22 ug/ml; range, 2.8 to 65.4). Cells derived from catecholamine-producing tumors were more sensitive to 6-OHDA than were those from non-catecholamine producers. By contrast, human fibroblasts, lymphoblastoid cell lines, and normal marrow were relatively insensitive to 6-OHDA; the concentration needed to kill 50% of cells for most of these cells exceeded 100 ug/ml. Leukemia cell lines and a rhabdomyosarcoma cell line were intermediate in sensitivity. Ascorbate and 6-OHDA were synergistic in toxicity for human neuroblastoma cells. Thus, in vitro addition of 6-OHDA and ascorbate was rapidly lethal for human neuroblastoma cells at concentrations which were minimally toxic for hematopoietic cells. This differential toxicity provides a possible means for selective destruction of neuroblastoma cells in bone marrow harvested for autologous transplantation. (Author abstract) (53 Refs)

27. HETEROGENEOUS CHEMOSENSITIVITIES OF SUBPOPULATIONS OF HUMAN GLIOMA CELLS IN CULTURE.

Yung WK, Shapiro JR, Shapiro WR

(c/o Shapiro), Cornell Univ. Medical Coll., 1275 York Ave., New York, NY, 10021

Cancer Res; 42(3):992-998 1982

Six karyotypically distinct clonal cell lines isolated from each of two freshly resected human malignant gliomas were examined for heterogeneity of morphology, in vitro growth rate, and chemosensitivity to 1,3-bis(2-chloroethyl)-1-nitrosourea and cis-diamminedichloroplatinum (II). Each clone was identified karyotypically as having come from the parent tumor. The karyotypic deviations were primarily numerical; chromosome numbers ranged from hypodiploid to near-tetraploid. Three morphological types were recognized: astrocyte-like; squamous-like; and fibroblast-like. The growth rates differed among the clones; the doubling times ranged from 48 to 84 hr in those from one tumor and from 72 to 252 hr in the other. Chemosensitivity was measured by cytotoxicity and/or colony-forming assay. In both assays and in both tumors, heterogeneity of chemosensitivity response to both drugs was demonstrated among the different clones from the same tumor. Dose-response curves from some clones differed statistically (log-probit analysis) from those of others, and when the curves were parallel, their 50% effective doses often differed. For the cytotoxicity assay, the 50% effective doses for BCNU ranged from 43 to 94 ug/ml and for cis-diamminedichloroplatinum (II), from 29 to 340 ug/ml. For the colony-forming assay, the 50% effective doses for 1,3-bis(2-chloroethyl)-1-nitrosourea ranged from 4.5 go 7.0 ug/ml and for cis-diamminedichloroplatinum (II), from 0.35 to 1.40 ug/ml. No correlation was evident between the chromosome number, morphology, growth rates, or chemosensitivities of the clones. These results identified heterogeneity of chemosensitivity among cellular subpopulations in human malignant gliomas. (Author abstract) (20 Refs)

28. COMBINATION CHEMOTHERAPY FOR THE 9L RAT BRAIN TUMOR MODEL SYSTEM.

Vats TS, Kimler BF, Henderson SD, Morantz RA

Dept. Pediatrics, Univ. Kansas Medical Center, Rainbow Blvd. at 39th St., Kansas City, KS, 66103

Cancer Treat Rep; 66(3):575-579 1982

Utilizing the 9L intracerebral rat brain tumor system, we have demonstrated that the combination of bleomycin delivered ic and BCNU (carmustine) given systemically is more therapeutically effective than either agent used alone. This benefit can be achieved without excessive short-term normal tissue damage. Furthermore, the potential for long-term normal tissue effects is reduced because of the low dose of bleomycin required. There was no difference between bleomycin given 16 hr before BCNU administration and the reverse sequence. These results suggest the possibility of adding intratumor bleomycin to protocols using BCNU for the treatment of malignant human brain tumors. (Author abstract) (8 Refs)

29. ADENOVIRUS-RELATED RNA SEQUENCES IN HUMAN NEUROGENIC TUMOURS.

Ibelgaufts H, Jones KW, Maitland N, Shaw JF
Institut fur Biochemie, Universitat Munchen, Karlstr. 23, D-8000 Munchen 2, W. Germany
Acta Neuropathol (Berl); 56(2):113-117 1982

A highly sensitive in-situ hybridization technique was used to detect adenovirus-related nucleic acids in 44 human neurogenic tumors. 3H-Labeled tumor virus DNA probes were derived from human adenovirus Type 2 and 12 (Ad2 and Ad12, respectively), bovine adenovirus Type 3 (BAd3), and avian adenovirus CELO. RNA sequences related to the adenovirus DNA probes used were not found in 10 tumors, three of which contained DNA that hybridized to Ad2 DNA only, 7 to Ad12DNA only, and 3 with BAd3 DNA only. Four tumors were positive for Ad2/Ad12 and three for Ad12/BAd3 simultaneously. Adenovirus-related RNA sequences were found in 2/3 astrocytomas, 2/4 metastatic carcinomas of the brain, 0.23 ependymomas, 2/2 glio blastomas. 1/1 secondary melanomas, 5/7 meningiomas, 4/4 neurinomas, 1/2 oligodendrogliomas, 0/1 pituitary chromophobe adenoma, and 1/1 rhabdomyosarcoma. No avian CELO virus-related RNA was detected in any of the tumors. No hybridization with viral DNA probes was observed in non-neoplastic control tissues. Thus, most brain tumors studied contained adenovirus-related material, predominantly RNA related to human adenovirus type 12. The finding of adenovirus-related RNA in 62% of the tumors tested is a lower estimate and their presence may reflect a viral involvement in the pathogenesis of these tumors. (18 Refs)

30. DNA VIRUSES AND BRAIN TUMOURS.

Ibelgaufts H
Chemisches Laboratorum, Institut fur Biochemie, Universitat Munchem, Karlstrasse 23, 800 Munchen 40, West Germany
Trends Neurosci; 5(1):16-20 1982

Evidence for viral involvement in pathogenesis of some human neurogenic tumors is reviewed. In the case of neurogenic tumor models, direct injection of the virus into the brain eliminates the potential for the host to clear the virus by the immune system. However, certain viruses, such as JCV human papovavirus and adenovirus type 12, can be used to induce intracerebral neoplasms by host infection other than intracerebral injection. Some human viruses (ie human adenovirus type 12 and human papovavirus JCV) are oncogenic both in rodents and in higher primates, however reasons for the differences in oncogenic potential between the various adenovirus serotypes is not known. Locations of the intracellular virus in DNA sequences have not been clearly defined, although some studies indicate that certain viral genes are only found at a limited number of sites; gene cloning techniques should help to evaluate the cellular sites of viral integration and their functions. Other studies suggest that viral genes are essentially fixed in the DNA sequence in virus-induced tumors. However, integrated viral genomes may be lost from transformed cells under certain circumstances. Presence of virus-specific RNA in virus-induced tumor cells is demonstrated by the presence of the so-called tumor(T)-antigen. Etiology of human neurogenic neoplasms is not clear, and proof of a viral etiology of human tumors must largely be circumstantial, yet there are observations that may point to tumor-virus involvement (eg adenovirus) in the pathogenesis of human neurogenic neoplasms. (15 Refs)

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CNS MALIGNANCIES

Diagnosis, Treatment

SERIES CT18 No. 82/09

SEPTEMBER, 1982

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NEUROGLIAL CELL TUMORS

1. THE BIOLOGICAL AND CLINICAL BEHAVIOUR OF PILOCYTIC ASTROCYTOMAS OF THE OPTIC PATHWAYS.

Borit A, Richardson EP
Lab. Neuropathology, Massachusetts General Hosp., Boston, MA, 02114

Brain; 105(part1):161-187 1982

Thirty cases of pilocytic astrocytoma were classified as either originating from an optic nerve (13) or optic chiasm

HE 20.3173/2:

(14); three cases had tumor mass in both regions. Age at onset of symptoms was 6 yr for pilocytic astrocytoma of chiasmatic origin and 3.5 yr for those originating in orbital optic nerves. Diagnostic procedures included cerebrospinal fluid evaluation, pneumoencephalogram, ventriculogram, and electroencephalogram (EEG). EEG abnormalities were frequent in both groups, but in the group of chiasmatic gliomas, an unfavorable prognosis was associated with EEG changes and seizures. Although surgery was the method of treatment in both types, 13/14 patients in the group with orbital gliomas have survived av 21.5 yr after surgery but only 8/16 chiasmatic glioma patients remain alive av 15 yr after surgery. A light and electron microscopic study of both tumor types showed identical histological features resembling those of hamartoma-like growths, among which aggressive behavior is exceptional. Overall, patients with orbital tumors did well, with or without recurrence of the tumor, but those with chiasmatic tumors did poorly due to tumor location: involvement with cerebral structures often prevented resection. The importance of differential diagnosis between reactive or hyperplastic astrocytes and those seen in low grade astrocytic neoplasm is emphasized. (44 Refs)

2. PATHOLOGICAL CORRELATION OF CT RING IN RECURRENT, PREVIOUSLY TREATED GLIOMAS.

Selker RG, Mendelow H, Walker M, Sheptak PE, Phillips JG
Dept. Neurosurgery, Univ. Pittsburgh, Montefiore Hosp., 3459 Fifth Ave., Pittsburgh, PA, 15213
Surg Neurol; 17(4):251-254 1982

The meaning of the enhancing ring commonly seen on computerized tomographic (CT) scans in patients with recurrent, treated glioblastoma has long been of concern. Does the ring represent radiation necrosis, pseudocapsule formation, compressed adjacent brain, or, in fact, a peripheral zone of viable tumor? We employed a multiple intratumoral biopsy technique at the time of reoperation to investigate this ring. Pathological evidence is presented documenting the content of the ring to be viable tumor. It is suggested that perhaps treatment failure may be determined on sequential CT examinations by comparing the volume and degree of contrast enhancement. (Author abstract) (12 Refs)

3. COMPUTED TOMOGRAPHY OF INTRACRANIAL EPENDYMOMAS.

Swartz JD, Zimmerman RA, Bilaniuk LT
Radiology Dept., Hosp. Univ. Pennsylvania, 3400 Spruce St., Philadelphia, PA, 19104
Radiology; 143(1):97-101 1982

Twenty-six patients with ependymoma were evaluated by computed tomography (CT) over a period of 5-1/2 yr. The usual CT appearance was an isodense, partially calcified mass, capable of contrast enhancement, occurring in the posterior fossa (73%) in an infant or child (77%). Outcome remains poor despite modern diagnostic and therapeutic methods. (Author abstract) (16 Refs)

4. TREATMENT OF MALIGNANT GLIOMA WITH MUMPS VIRUS.

Yumitori K, Handa H, Yamashita J, Suda K, Otsuka S, Shimizu Y
Dept. Neurosurgery, Faculty Medicine, Univ. Kyoto, Kyoto, Japan
No Shinkei Geka; 10(2):143-147 1982

Six patients with malignant brain tumor were treated with mumps virus. Mumps virus was considered to be effective in three cases which were described in detail. First case: A 51-yr-old male with glioblastoma in the left thalamus was treated unsuccessfully with irradiation and chemotherapy after partial removal of the tumor. Mumps virus was administered, and 3 wk later showed 62% decrease of the tumor. Fifteen mo have passed since the treatment was started and the patient is still alive. Second case: A 46-yr-old male with a tumor in the corpus callosum was irradiated without operation. There was a 95% increase of the tumor. Mumps virus was administered, the tumor disappeared almost completely. The patient died 1 yr after the treatment was started, and death is ascribed to the metastatic lesion in the posterior fossa. Third case: An 18-yr-old female had a mass lesion in the left frontal lobe adjacent to the anterior horn of the lateral ventricle. Partial removal was performed and histological diagnosis was a mixed glioma consisting of ependymoma and oligodendroglioma. She was treated with mumps virus alone postoperatively. Follow-up CT scans showed an almost complete disappearance of the tumor. In the third case, administration of mumps virus alone induced an almost complete disappearance of the tumor on CT scans and improvement of clinical state. No effect of mumps virus was observed in other cases. The mechanism how mumps virus acts on tumor-bearing patients is not established but immunological effect appears to be most likely. Several immunological parameters such as NK cell, killer T-cell, suppressor T-cell function and specific reaction to TSA will be examined. (9 Refs) (In JPN)

NEURONAL CELL AND PRIMITIVE BIPOTENTIAL PRECURSOR CELL TUMORS

5. COMPUTERIZED TOMOGRAPHIC FINDINGS IN MEDULLOBLASTOMAS.

Weisberg LA
Tulane Medical Center, New Orleans, LA, 70112
Comput Radiol; 6(2):83-91 1982

Computerized tomography (CT) was performed in 20 patients (8 female, 12 male; 11 mo -23 yr old) with intracranial medulloblastomas (MB). All presented with headache, 13 with vomiting, 12 with gait instability, 6 with double vision, 3 with lethargy, and 1 with dysphagia. Average duration of symptoms prior to diagnosis of MB by CT was 8 wk (range 4-16 wk). Neurological findings are given, and the pattern of neurological dysfunction correlated well with location of the MB. In 16 cases the MB appeared as a posterior fossa midline lesion, and in 4 cases it was located laterally. Obstructive hydrocephalus was universal. Non-contrast CT showed 14 of the cases to be hyperdense (only 1 with calcification) and 6 to be isodense. Subsequent post-contrast CT showed enhancement in all cases, 18 homogeneous and 2 ring-patterns. All cases showed third and lateral ventricular dilatation, and abnormalities of the fourth ventricle. A surrounding hypodense rim was seen in 12 cases. (7 Refs)

6. ADJUVANT CHEMOTHERAPY WITH PROCARBAZINE, VINCRISTINE AND PREDNISONE FOR MEDULLOBLASTOMAS: A PRELIMINARY REPORT.

Seiler RW, Bernasconi S, Berchtold W, Feldges A, Imbach P, Luthi A, Pluss HJ, Vassella F, Wyss M, Wagner HP
Dept. Neurosurgery, Univ. Hosp., CH-3010 Bern, Switzerland
Helv Paediatr Acta; 36(3):249-254 1981

Following complete tumor resection, 20 children (less than 16 yr old) with confirmed medulloblastomas were given craniospinal radiotherapy (RT: 5,000-6,500 rads to the posterior fossa, 3,500-4,500 rads to the rest of the brain, and 3,000-3,500 rads to the spinal cord). Chemotherapy with procarbazine (150 mg/square meter [m2]/day x 14, po) vincristine (VCR: 1.5 mg/m2/wk x 3, iv), and prednisone (PRN: 40 mg/m2/day x 14, po) was initiated 2 mo after the end of RT and repeated every 6 wk for 8 cycles. Four patients died during chemotherapy (at least 4 courses); none died of toxicity. The other 16 patients were given the full course of chemotherapy, with appropriate dose modifications when side effects developed. Follow-up times were 18-56 mo after tumor resection. The survival rates were 89% at 1 yr, 53% at 2 yr, 44% at 3 yr, and 39% at 4 yr. These survival rates were comparable to those observed in 231 patients treated only with RT (71-74% at 1 yr, 58-60% at 2 yr, 42-50% at 3 yr, and 35-50% at 4 yr). Higher survival rates have been reported for 142 children treated with VCR and lomustine (CCNU, with VCR beginning during RT: 85% at 1 yr, 70% at 2 yr, 62% at 3 yr, and 58% at 4 yr) and 83 children treated with VCR (beginning during RT), CCNU, and PRN (during induction only: 79% at 1 yr, 68% at 2 yr, 65% at 3 yr, and 56% at 4 yr). In this multi-institutional study, the best results were observed among children treated at large medical centers which treated at least 20 pediatric medulloblastoma patients/yr. The experience of the neurosurgeons and radiation oncologists probably influenced the treatment results. (8 Refs)

TUMORS OF THE CRANIAL AND SPINAL NERVE ROOTS

7. CEREBROSPINAL FLUID 'LEAKS' AND MENINGITIS FOLLOWING ACOUSTIC TUMOR SURGERY.

Hughes GB, Glasscock ME, Hays JW, Jackson CG, Sismanis A
(c/o Glasscock) Otology Group, P. C., 1811 State St., Nashville, TN, 37203
Otolaryngol Head Neck Surg; 90(1):117-125 1982

Of 271 intracanalicular and cerebellopontine angle lesions reviewed, 237 were removed by the translabyrinthine or combined approach which created a mastoid defect. These 237 patients were divided into three groups: 188 patients' defects were obliterated using older techniques of packing the eustachian tube with muscle or bone and removal of the incus (Group A); 16 patients had no obliteration of the mastoid defect (Group B); and 33 patients had obliteration of the defect and closing of the wounds by newer packing and closing techniques (Group C). The incidence of cerebrospinal fluid (CSF) leakage in Group A was 25% and meningitis occurred in 16%. In Group B, CSF leakage occurred in 50% and meningitis in 25%. In Group C, CSF leakage and meningitis occurred in 6%. Four major problem areas were identified: the eustachian tube, the middle ear, the mastoid defect, and the postauricular wound. Of these, the most important in minimizing postoperative CSF wound leakage, CSF rhinorrhea, and meningitis was obliteration of the mastoid defect. Previous obtained rectus fascia was used to line the defect and abdominal fat was packed within the fascial sling to the level of the cortical bone surface; this separates the subarachnoid space from areas of the middle ear and the postauricular wound. Careful packing of the eustachian tube and middle ear, obliteration of the mastoid defect, and reinforced closure of the postauricular wound effectively reduced the incidence of CSF leakage and meningitis. (11 Refs)

TUMORS OF THE LYMPHORETICULAR SYSTEM AND BLOOD VESSELS

8. CAROTID BODY TUMORS IN HUMANS: GENETICS AND EPIDEMIOLOGY.

Parry DM, Li FP, Strong LC, Carney JA, Schottenfeld D, Reimer RR, Grufferman S
Clinical Epidemiology Branch, Div. Cancer Cause and Prevention, NCI, NIH, Public Health Services, Landow Building, Room 5A21, Bethesda, MD, 20205
JNCI; 68(4):573-578 1982

Genetic factors in the etiology of carotid body tumors (CBT) were sought in a medical record review of 222 histologically diagnosed cases at 12 US medical centers. Patients in the series, which had a marked female predominance (146 females:76 males), usually developed tumors between the fourth and seventh decades of life (mean, 44.7 yr). In 16 patients who also had other extra-adrenal paragangliomas, suggesting a multiple primary tumor syndrome, CBT were diagnosed significantly earlier (mean, 35.4 yr; p less than 0.01). The occurrence of thyroid cancer in five other patients appeared to be excessive. Familial CBT was recognized in 16 patients from 13 affected families, including 9 newly ascertained kindreds. Compared with nonfamilial lesions, familial CBT tended to develop bilaterally (38% vs 8% unilaterally) and at slightly earlier ages (41.6 vs 44.9 yr). CBT was reported to occur in an autosomal dominant pattern in some families and within sibships in others; relatives were not examined for confirmation. The familial findings are generally consistent with a two-step mutation model of the development of hereditary and nonhereditary CBT; apparent deviations from the model might be clarified with additional data on this rare neoplasm. (Author abstract) (35 Refs)

9. CT FINDINGS IN CEREBELLAR HEMANGIOBLASTOMAS.

Heiss E, Albert F
Neurochirg. Klinik, Univ. Erlangen-Nurnberg, Schwabachanlage 6, D-8520 Erlangen, W. Germany
RGEFO; 136(2):151-156 1982

The computed tomographic (CT) findings in 16 personal cases of cerebellar hemangioblastomas are presented. According to other reports in the literature, three-quarters of the tumors were cystic, containing a small mural nodule, whereas the others were predominantly solid. By CT scan the cystic tumors were always identified as roundish or oval space-occupying lesions, sharply demarcated from the surrounding tissue. The solid portion of these tumors, projecting into the cystic part, was delineated more precisely by contrast enhancement, but sometimes escaped identification. On the contrary, even after contrast enhancement the predominantly solid tumors could not be clearly identified as hemangioblastomas. Calcification could not be demonstrated. Additional angiographic investigations were imperative in order to establish the diagnosis, besides visualizing further hypervascular nodules of hemangioblastoma, which CT scanning failed to reveal. (Author abstract) (31 Refs) (In GER)

SECONDARY TUMORS OF THE CNS

10. COMPUTED TOMOGRAPHIC DEMONSTRATION OF THE EFFECTS OF BROMOCRIPTINE ON PITUITARY MICROADENOMA SIZE.

Bonneville JF, Poulignot D, Cattin F, Couturier M, Mollet E, Dietemann JL

Dept. Neuroradiology, Univ. Hosp. Besancon, 25030 Besancon, France

Radiology; 143(2):451-455 1982

A group of 17 strictly intrasellar prolactin-secreting pituitary adenomas between 2 and 9 mm in size was examined by computed tomography before and after bromocriptine therapy of 3 mo to 1 yr duration. These findings were compared with clinical and biological data. Bromocriptine therapy was effective clinically and biologically in 14 of the 17 cases. Of the 15 intrasellar adenomas in nonpregnant patients treated with bromocriptine, 6 disappeared completely with normalization of the pituitary appearance, 5 decreased approx 50% in volume, (3 showed an increase in density, 2 a decrease), and 4 remained unchanged in size (2 showed increased density, 2 showed very low densities). (Author abstract) (13 Refs)

11. ADENOMA OF THE HUMAN PITUITARY PRODUCING GROWTH HORMONE AND THYROTROPIN. A HISTOLOGIC, IMMUNOCYTOLOGIC AND FINE-STRUCTURAL STUDY.

Kovacs K, Horvath E, Ezrin C, Weiss MH

Dept. Pathology, St. Michael's Hosp., Univ. Toronto, 30 Bond St., Toronto, Ontario, Canada

Virchows Arch [Pathol Anat]; 395(1):59-68 1982

A pituitary adenoma removed by surgery from a 22-yr-old man was studied by histology, immunocytology, transmission electron microscopy and immunoelectron microscopy. Clinically, the patient had acromegaly and euthyroidism with elevated blood GH concentrations. Blood TSH and T4 levels were within the normal range. Histologically, the adenoma was chromophobic and exhibited no PAS, lead hematoxylin, aldehyde thionin or Grimelius silver positivity. By the immunoperoxidase technique GH, beta-TSH and alpha-subunit but no PRL, ACTH, alpha-endorphin, beta-FSH or beta-LH were demonstrated in the adenoma cells. Electron microscopy revealed adenoma cells which were similar to TSH cells and showed no resemblance to GH cells of nontumorous pituitaries or GH-secreting tumors. Immunoelectron microscopy demonstrated GH and beta-TSH in the secretory granules. It is concluded that pituitary adenomas composed of TSH-like cells may secrete GH, resulting in acromegaly. Production of GH by adenomatous TSH cells cannot be explained on the basis of the one cell- one hormone theory. The question is raised whether bihormonal or multihormonal clones, capable of synthesizing more than one hormone, exist in the human pituitary. These cells are apparently dormant under normal conditions, but in the course of neoplastic transformation may undergo functional dedifferentiation and acquire the ability to produce two or more different hormones. (Author abstract) (33 Refs)

12. TRANSSPHENOIDAL MICROSURGICAL REMOVAL OF GROWTH HORMONE-SECRETING PITUITARY ADENOMAS.

Baskin DS, Boggan JE, Wilson CB

Dept. Neurological Surgery, Editorial Office, Univ. California Sch. Medicine, 350 Parnassus Ave. Suite 807, San Francisco, CA, 94117

J Neurosurg; 56(5):634-641 1982

A series of 137 patients with growth hormone (GH)-secreting pituitary adenomas were treated by transsphenoidal surgery during a 10-year period. Group A comprised patients for whom this surgery was the first therapeutic intervention, and Group B included those who underwent the surgery after previous therapeutic intervention. The results were analyzed considering preoperative and postoperative endocrinological, neurological, ophthalmological, and neuroradiological data. Remission was defined as clinical response and a normal postoperative GH level, and partial remission as clinical response and postoperative reduction of the GH level by more than 50%. Any other result was considered failure. The mean follow-up period was 37.1 months; follow-up review was achieved in all the patients. Among the 120 patients in Group A, remission was achieved in 80 (78%) patients with transsphenoidal surgery alone, and in an additional 16 (16%) after postoperative irradiation (combined response rate, 94%). All failures and patients with partial remission had preoperative GH levels of more than 50 ng/ml and suprasellar extension of the tumor. There were no deaths; 8% of patients had minor surgical morbidity; 5% had new hypopituitarism postoperatively. Of patients subsequently irradiated, 71% developed hypopituitarism. Among the 35 patients in Group B, remission was achieved in 26 (74%), partial remission was obtained in 2 (6%), and 7 (20%) were considered treatment failures. There were no deaths, and the morbidity rate was 14%; 66% of patients had hypopituitarism postoperatively. Of the eight patients who had received prior irradiation only, seven (88%) went into remission. All failures and partial responders had preoperative GH levels greater than 40 ng/ml; 56% had suprasellar extension. These results confirm the efficacy of the transsphenoidal approach for the treatment of GH-secreting pituitary adenomas. (Author abstract) (49 Refs)

13. TRANSSPHENOIDAL REMOVAL OF PITUITARY TUMORS: EXPERIENCE WITH 167 PATIENTS.

Tucker HS, Grubb SR, Wigand JP, Taylon A, Lankford HV, Blackard WG, Corales RL, Becker DP

Box 111, Medical Coll. Virginia Station, Richmond, VA, 23298

Va Med; 109(3):164-170 1982

Experience with transsphenoidal removal of pituitary tumors in 67 patients is reported. The operative approach used was that of Hardy, employing an operating microscope. Intraoperative fluoroscopic monitoring was used in cases with macroadenomas with significant extension. Wide bony exposure of the floor of the sella turcica was important. Complete inspection of the sella contents was conducted prior to removal of microadenomas. For larger adenomas with significant suprasellar extension, removal was facilitated by using a sustained Valsalva maneuver. Of 67 women with prolactin-secreting tumors, 44 were cured and 1 developed hypopituitarism (HOP). Of 40 patients with growth hormone-secreting tumors and acromegaly, 30 were cured and 4 developed HOP. Of 12 with Cushing's disease, 10 were cured and 1 died from surgery. Of six patients with Nelson's syndrome, four were cured. No cure was observed in the one patient with a thyroid-stimulatng hormone secreting tumor. Of 41 patients with large nonsecreting tumors or prolactin-secreting tumors, 20 were cured , 1 developed HOP, and 1 died from surgery. (14 Refs)

14. THERAPEUTIC EFFECT ON GALACTORRHEA AND STERILITY IN PROLACTIN-SECRETING PITUITARY ADENOMAS.

Sato O, Tanabe S, Tsuchita H, Nakagawa T, Inoue Y, Daibo M, Uede T, Hotta H
Dept. Neurosurgery, Sapporo Medical Coll., Sapporo 060, Japan
Neurol Med Chir (Tokyo); 21(11):1123-1133 1981

The authors investigated factors responsible for cessation of galactorrhea or restoration of ovulation in 30 women with PRL-secreting pituitary adenomas after surgery with or without bromocriptine. All the patients complained of sterility and 25 patients had galactorrhea. Microsurgical removal of adenomas was performed in all the patients and 15 patients received oral bromocriptine after surgery on account of sustained elevated serum PRL levels. Galactorrhea ceased in 19 out of 25 patients (76.0%) after the treatment. Preoperative serum PRL levels, age of patients at surgery, duration of galactorrhea, history of nursing, severity of galactorrhea and serum estradiol or progesterone levels had no correlation with cessation of galactorrhea. Ovulation was restored in 18 of 30 patients (60.0%) after the treatment and pregnancy was established in 12 patients. The PRL levels where ovulation was restored ranged from there to 57 ng/ml. The normal PRL levels did not inevitably ensure restoration of ovulation. There was no difference in the frequency of restoration of ovulation after the treatment between patients with preoperative PRL levels below 200 ng/ml after surgery. There was a prevalence in the frequency of restoration in amenorrhea Grade I, preoperative duration of sterility of less than 5 yr, microadenomas, a longer postoperative interval normal serum basal LH levels and peak LH levels in response to LH-RH and the presence of positive feedback control to surge LH in response to estrogen. Age of the patients at surgery, elevated dopamine activity in the hypothalamus and serum estradiol or progesterone levels were not correlated with restoration of ovulation. (36 Refs) (In JPN)

OTHER THERAPY OF CNS MALIGNANCIES

15. HUMAN CENTRAL NERVOUS SYSTEM DISTRIBUTION OF CIS-DIAMMINEDICHLOROPLATINUM AND USE AS A RADIOSENSITIZER IN MALIGNANT BRAIN TUMORS.

Stewart DJ, Leavens M, Maor M, Feun L, Luna M, Bonura J, Caprioli R, Loo TL, Benjamin RS
(c/o Benjamin) Dept. Developmental Therapeutics, M. D. Anderson Hosp., Houston, TX, 77030
Cancer Res; 42(6):2474-2479 1982

The human central nervous system pharmacology of cis-diamminedichloroplatinum (CDDP) was studied, and trials were initiated of CDDP as a radiosensitizer in the treatment of malignant primary brain tumors. Samples were assayed for platinum using x-ray-dispersive fluorescence spectrometry. Platinum concentrations in edematous brain tissue adjacent to tumor were generally lower than platinum concentrations in intracerebral tumor. Brain platinum concentration decreased with increasing distance from intracerebral tumor. The extent to which central nervous system pharmacology of an antineoplastic agent affects its activity against intracerebral neoplasms remains unclear. Fifteen patients with malignant brain tumors received CDDP, 40 mg/sq m/wk iv during cranial irradiation, and some received 105 to 120 mg/sq m every 3 wk after cranial irradiation. Close follow-up was necessary, and some weekly treatments needed to be omitted in individual patients. During the weekly CDDP, gastrointestinal, scalp, and renal toxicities and hypomagnesemia were noted but were tolerable. Only one patient developed myelosuppression. Ototoxicity may have been enhanced. Postirradiation CDDP, 105 to 120 mg/sq m every 3 wk, caused substantially more gastrointestinal toxicity and may have caused central nervous system toxicity in four patients, although other factors probably contributed. It is too early to evaluate effect on survival. (26 Refs)

16. INTERFERON THERAPY FOR BRAIN TUMOR PATIENTS.

Ueda S, Hirakawa K, Suzuki K, Nakagawa Y, Ibayashi N, Kishida T
Dept. Neurosurgery, Kyoto Prefectural Univ. Medicine, Kyoto, Japan
No Shinkei Geka; 10(2):149-154 1982

Nine cases of recurrent and metastatic brain tumors were treated by human interferon-alpha (Hu-IFN-alpha). It was given intramuscularly and singly to those who finished the usual treatments of surgical removal and 60Co irradiation more than 6 mo before, to exclude their effects on tumors. They were divided into two groups of small dosage (50,000 units weekly) and large dosage (3,000,000 units every other day). The total dosage of IFN varied from about 2,000,000 units for the small dosage group to 264,000,000 units for the large dosage group. No side effects were noted. In two cases of six which were followed up over 4 mo, the tumors regressed about 50% on serial CT. However, IFN was not effective on the tumors which had already showed a rapid growth before IFN administration. Almost all the patients showed improvements in their general condition, PPD and PHA skin test, peripheral lymphocyte counts and natural killer cell activities. (Author abstract) (14 Refs) (In JPN)

17. HYPERTHERMIA IN CANCER THERAPY: POTENTIAL APPLICATION TO BRAIN TUMORS.

Tanaka R
Dept. Neurosurgery, Brain Res. Inst., Niigata Univ., Niigata, Japan
No Shinkei Geka; 10(1):7-19 1982

Concepts involved in the application of hyperthermia to cancer therapy were introduced, and problems with hyperthermia and its future development as a method for treatment of tumors were discussed. Basic biological studies of hyperthermia indicate that hyperthermia affects tumor tissues because of the following reasons: selective sensitivity of tumor cells to heat, which influences respiration and glycolysis, synthesis of nucleic acids and proteins, and lysosomes; immediate cell killing; and delayed cell killing. Using rats bearing Rous sarcoma virus-induced brain tumors and monkeys with primary brain tumors, radiofrequency hyperthermia (13.56 megaH) produced marked antitumor effects. Since the tumor cell:normal surrounding cell temperature difference was as high as 8-10 C, it was thought that hyperthermia as high as 48-50 C would be attainable in the brain (due to cerebral blood flow, the brain maintains a steady temperature of 40 C). Compared to the use of radiotherapy or chemotherapy alone, combinations of hyperthermia and 60Co radiotherapy or of hyperthermia and chemotherapy prolonged the growth times of tumors, suggesting possible combinations of therapies that might be effective in clinical settings. With advances in hyperthermia apparatuses, treatment of brain tumors with hyperthermia was thought to be possible in the future. (90 Refs) (In JPN)

OTHER CLINICAL ASPECTS OF CNS CANCER

18. DIAGNOSTIC VALUE OF BRAIN STEM AUDITORY EVOKED POTENTIALS.

Fischer C, Blanc A, Mauguiere F, Courjon J
Hopital Neurologique, 59, boulevard Pinel, F 69003 Lyon, France
Rev Neurol (Paris); 137(4):229-240 1981

Brain stem auditory evoked potentials (BAEP) were included in the examination of 155 patients with suspected or proven multiple sclerosis (MS), of 25 who had had a cerebral vascular accident, and of 66 with suspected or proven brain tumors. Of the 155 possible MS patients, 57 had abnormal BAEP. Of the 33 patients with proven MS, 22 had abnormal BAEP. In certain cases, particularly those of vascular origin, BAEP value was limited to confirmation of clinical observations. BAEP findings were normal in numerous patients with brain stem abnormalities including four young subjects with large mesencephalic angiomas. Cerebellar tumors (5 cases), meningiomas of the posterior cerebral fossa (8), and other tumors tested produced BAEP abnormalities that increased as a function of tumor volume and relation to auditory tracts. When the tumor was detectable by computed tomography, BAEP was useful in pointing out the exact relationship of the tumor to the auditory tracts. In 36 patients with suspected or proven tumors, BAEP provided useful diagnostic information. In 33 patients with suspected brain stem tumors, BAEP findings were very abnormal in 4 who were later found to have brain stem tumors (1 by computed tomography, 1 by surgical biopsy, and 2 at autopsy). In 15/33 patients, normal BAEP findings virtually precluded any brain stem tumor. In 14/33 patients, BAEP findings were not conclusive. The value of BAEP in differential diagnosis of brain stem abnormalities is discussed. (16 Refs) (In FRE)

19. CONTRIBUTION OF BRAINSTEM AUDITORY EVOKED POTENTIALS TO DIAGNOSIS OF TUMORS AND VASCULAR DISEASES.

Fischer C, Mauguiere F, Echallier JF, Courjon J
Hopital Neurologique, 69394 Lyon, France
Adv Neurol; 32:177-185 1982

Brainstem auditory evoked potentials (BAEP) were measured in 25 patients with known vascular diseases and 66 patients with suspected or confirmed mesencephalic or rhombencephalic tumors (excluding acoustic neuromas). The BAEP test provided useful diagnostic information on 36/66 patients with suspected tumors. It was particularly useful in 33 patients with suspected brainstem tumors, in whom computed tomography (CT) had either confirmed nor eliminated the possibility of a brainstem tumor. Normal BAEPs in 14/33 patients cast doubt on the likelihood of brainstem tumor, and this was confirmed by the results of follow-up for nearly 2 yr in all patients. In 14 other patients, the CT scans suggested either a brainstem tumor or a first brainstem tumor relapse of multiple sclerosis (MS). The normal BAEP in these patients ruled out brainstem tumors but left the diagnosis of MS in doubt. Four patients showed very large BAEP abnormalities and were later diagnosed as having infiltrative brainstem tumors. In 13 patients with cerebellar tumors (5/13) or posterior fossa meningiomas (8/13), the extent of BAEP abnormalities depended on the tumor's vol and especially its relationship to the auditory pathways. Since these tumors had already been detected by CT scans, the additional information provided by BAEP was usually small; however, BAEP could provide useful information for treatment planning. In many patients with vascular diseases, the BAEP findings only confirmed the clinical findings. The significance of wave VI (whose presence coincides with the integrity of the median geniculate body, but which is absent in nearly 50% of normal persons) and the problem of the ipsilateral or contralateral origin or wave V on the BAEP are discussed. (16 Refs)

20. DIAGNOSTIC SIGNIFICANCE OF CORTICAL SOMATOSENSORY EVOKED POTENTIALS FOLLOWING TRIGEMINAL NERVE STIMULATION.

Buettner UW, Petruch F, Scheglmann K, Stohr M

Dept. Neurology, Univ. Tubingen, D-7400 Tubingen, W. Germany

Adv Neurol; 32:339-345 1982

Pathologically prolonged or abnormally shaped trigeminal somatosensory evoked potentials (T-SEP) were observed in patients with trigeminal neuralgia who had not been treated surgically; in 28/46 patients with multiple sclerosis (although 18/26 had no clinical symptoms of trigeminal nerve demyelination); in 6/7 patients with brainstem ischemia (indicating involvement of the main sensory nucleus in a majority of patients); and in 6/11 patients with tumors of the cerebellopontine angle (indicating trigeminal nerve compression by the tumors). It is suggested that the addition of T-SEP examinations to standard diagnostic procedures can help to determine the extent of a disease before invasive diagnostic procedures are performed. (8 Refs)

21. THE PATTERN-REVERSAL VISUAL EVOKED POTENTIAL IN THE CLINICAL STUDY OF LESIONS OF THE OPTIC CHIASM AND VISUAL PATHWAY.

Camacho LM, Wenzel W, Aschoff JC

Dept. Neurology, Univ. Ulm, Ulm, W. Germany

Adv Neurol; 32:49-59 1982

Visual evoked potentials (VEP) and pattern-reversal (PR) responses were studied, using midline electrode positions, in 18 patients with abnormal masses of the optic chiasm (OC: 9/18) or parieto-occipital region (POR: 9/18), as revealed by computed tomography (CT), angiography, or surgery. Postoperative follow-up VEP studies were performed in some patients. Bitemporal hemianopia was present in 5/9 patients with OC mass and homonymous hemianopia in 7/9 patients with POR masses. The PR responses were abnormal in 8/9 patients with OC masses. Stimulation of the temporal retina led to abnormal responses even in the absence of visual field defects. Demyelination caused by nerve compression (confirmed at surgery in these patients) was thought to be the cause of these abnormalities. A good correlation was noted between abnormal VEP responses and the results of CT scans and surgery. Amplitude was diminished in the early stages of the disease, and the response was delayed or absent in the later stages. The VEP responses were abnormal in 8/9 patients with POR masses (prolonged latencies and small amplitudes in 4/9, absent responses in 4/9), after stimulation of the half-fields contralateral to the location of the mass. These abnormalities were observed in the presence or absence of visual field defects, and could not be used to distinguish between cerebrovascular diseases and tumors. A good correlation was noted between the clinical findings and the VEP and PR results. It is suggested that these examinations may be useful in the detection and location of masses of the visual pathway (perhaps including clinically occult disease in some patients) and in postoperative follow-up studies. (24 Refs)

SELECTED PRECLINICAL ASPECTS OF CNS CANCER

22. AGE-RELATED CHEMOSENSITIVITY OF STEM CELLS FROM HUMAN MALIGNANT BRAIN TUMOURS.

Rosenblum ML, Gerosa M, Dougherty DV, Reese C, Barger GR, Davis RL, Levin VA, Wilson CB
Brain Tumor Res. Center, Dept. Neurological Surgery, Univ. California Sch. Medicine, San Francisco, CA, 94143
Lancet; 1(8277):885-887 1982

After radiation therapy and chemotherapy for malignant glioma, patients aged 50 or under survive longer than patients over 50. Data from Brain Tumor Study Group trials show that, without treatment, these age groups have similar survival; therefore unperturbed tumor growth does not account for the difference. Sixteen consecutive patients with malignant glioma were studied, half of whom were less than or equal to 50 years of age; none had been treated before initial surgery, and all were subsequently treated with radiation and chemotherapeutic agents (in all but 2 patients, with nitrosoureas). Median survival of those aged less than or equal to 50 years was 54 + weeks whereas that of those aged greater than 50 was 37 weeks. The longer survival for younger patients could not be attributed to tumor type, size, or location, pretreatment Karnofsky status, or mode of treatment. In-vitro sensitivity testing of clonogenic cells obtained from biopsy specimens showed that tumor cells from seven of eight patients aged less than or equal to 50 years were sensitive to 1,3-bis (2-chloroethyl)-1-nitrosourea (greater than 40% cell kill at clinically achievable concentrations) compared with only one patient with sensitive cells out of eight older patients. Patient age was inversely correlated with in-vitro cell kill, and patients with sensitive cells were significantly younger than those with resistant cells. Therefore influence of age on survival after treatment of malignant gliomas is probably due to inherent differences in the sensitivity of clonogenic cells to radiation and/or chemotherapeutic agents. (Author abstract) (25 Refs)

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NEUROGLIAL CELL TUMORS

1. IMMUNOREGULATORY CELL STUDIES IN PATIENTS WITH GLIOMAS (MEETING ABSTRACT)

Penn RD, Showel J, Harris JE, Braun DP, Wolter JW
Rush-Presbyterian-St. Luke's Medical Center, Chicago, IL, 60612
Proc Am Assoc Cancer Res; 23:990 1982

Indomethacin-sensitive, glass adherent, and preculture sensitive immunoregulatory activity was measured in the peripheral blood mononuclear cells (PBMC) from 16 patients with glioblastoma multiforme (glioma) tumors. Levels of immunoregulatory cell function were determined in assays of phytohemagglutinin (PHA) induced lymphocyte DNA synthesis and expressed as an augmentation index (AI) calculated as the cpm per culture of indomethacin-treated, glass adherent cell depleted, or 24-hour precultured PHA-stimulated cultures divided by the cpm per culture of nonmanipulated, PHA-stimulated cultures. Individual patient values were considered to be significantly different from normal when the AI for the patient sample fell greater than 2 standard deviations above the mean AI determined for a group of 10 age matched normal subjects. Of 8 patients studied prior to surgical exploration and diagno-

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sis, 8 were found to exhibit significantly depressed levels of PHA responsiveness in association with significantly increased levels of regulatory cell function by glass adherent, preculture-sensitive and/or indomethacin-sensitive cells. Eight patients were studied following diagnosis and treatment. Of those, 3 patients in remission had normal levels of immune function in association with normal levels of regulatory cell activity, 3 patients with active recurrent disease had significantly depressed T cell function in association with increased regulatory cell activity and 2 patients with active recurrent disease had normal levels of immune function in association with normal levels of regulatory cell activity. The changes in regulatory cell function seen in PBMC from glioma patients prior to surgical biopsy or following active tumor recurrence could not be correlated with levels of immune complexes in patient sera. These data suggest that increased levels of regulatory cell function by glass adherent, preculture sensitive and/or indomethacin-sensitive cells contribute to the impaired immuno-competence of glioma patients. (no Refs)

2. GANGLIONEUROBLASTOMA: HISTOLOGIC PROGNOSTIC FACTORS (MEETING ABSTRACT)

Shimada H, Hamoudi AB, Newton WA
Columbus Children's Hospital, Columbus, OH
Lab Invest; 46(1):14P 1982

This study is a review of 40 patients with ganglioneuroblastoma (GNB) selected from a total of 215 who had sufficient histologic material from the primary lesion before treatment with chemotherapy and/or radiation therapy. These cases were subdivided histologically into four groups: (1) well-differentiated GNB: has same appearance of ganglioneuroma except for a presence of a few relatively premature gangliocytes, (five patients); (2) multifocal GNB: these tumors have the appearance of ganglioneuroma with presence of multiple small foci of neuroblastic tissue of various degrees of maturation. These foci blend with surrounding tissue without a capsule (10 patients); (3) composite GNB: they are characterized by the presence of one or more large discrete nodules of premature neuroblastic tissue. This nodule(s) is very large and usually separated from surrounding ganglioneuroma tissue by a capsular structure, (eight patients); (4) differentiating GNB: composed of a mixture of neuroblastic cells with different degrees of maturation without presence of ganglioneuromatous elements. They might have nodular appearance (17 patients). This histologic subgrouping is easy and reproducible. The prognosis of patients with well-differentiated GNB was good. The prognosis of patients with multifocal GNB was very good regardless of age or stage of the disease. On the other hand, the prognosis of patients with the composite type was poor regardless of stage or age. The 10 patients with multifocal GNB are alive and well except for one, whereas the eight patients with composite type are all dead. The differentiating GNB appeared to have a variable prognosis. (no Refs)

3. MALIGNANT GLIOMA: A RANDOMIZED TRIAL OF RADIOTHERAPY PLUS BCNU, PROCARBAZINE, OR DTIC; A SWOG STUDY (MEETING ABSTRACT)

Eyre HJ, Eltringham JR, Quagliana JM, Lane DM, Frank J, Vogel FS
University of Utah, Salt Lake City, UT, 84132
Proc Am Soc Clin Oncol; 1:C-701 1982

This prospective randomized clinical trial compared radiotherapy (XRT) (6000 rads/7 wks) plus either BCNU (carmustine) (80 mg/m(2)/day IV x 3 q 6 wks), Procarbazine (PCZ) (100 mg/m2 po/day) or DTIC (dacarbazine) (175 mg/m2 IV/day x 5 q 4 wks) following surgery in the treatment of patients with histologically proven malignant gliomas. All patients also received dexamethasone 10 mg/m(2)/day during radiation. Two hundred and seventy-two eligible patients have been entered. Entry of patients was stratified by age, tumor grade, and extent of surgery resulting in comparable groups. The overall response rates are statistically significantly different. The difference is due to the low response rate of PCZ. There are no differences between the treatments in duration of response or survival. However, when survival on the BCNU limb is compared to the PCZ limb, PCZ may be inferior. Age was the most important prognostic factor identified. Significant myelosuppression and gastrointestinal toxicity were observed in each of the treatments with 9 toxic deaths. Allergic reactions to PCZ were common; 11 patients were taken off study because of intense drug rashes. This study suggests that daily oral PCZ is inferior to BCNU in the treatment of malignant gliomas. (no Refs)

4. RADIATION THERAPY (RT) AND BCNU WITH AND WITHOUT MISONIDAZOLE FOR MALIGNANT GLIOMA, PRELIMINARY RESULTS OF A RANDOMIZED CLINICAL TRIAL. AN RTOG STUDY (MEETING ABSTRACT)

Nelson DF, Schoenfeld D, Weinstein AS, Carabell SC
University of Pennsylvania, Philadelphia, PA, 19104
Proc Am Soc Clin Oncol; 1:C-768 1982

Misonidazole, a hypoxic-cell radiosensitizer, has been used in a prospective randomized trial (RTOG 79-18) for treatment of malignant glioma since November 1979. By September 1981, 173 eligible patients were entered on study, with follow-up information available on 165 cases. Whole brain conventional RT (170-200 rads/fraction to 6000 rads) was compared to Misonidazole sensitized radiotherapy (6000 rads delivered as 400 rads on Mondays, 150 rads Tuesday, Thursdays and Fridays to 5100 rads plus 900 rad in 5 fractions). Six doses of 2.5 gm/m2 Misonidazole were administered 4-6 hours before the 400 rads dose. Both treatment groups received BCNU (carmustine) 80 mg/m2 for 3 days every 8 weeks. With a median follow-up (FU) of 8 months 35% of the patients have died. The difference in survival between the 2 arms is not statistically significant. Misonidazole toxicity included neuropathy in 13% of the patients (4% moderate and 9% mild), severe nausea and vomiting in 13% and mild to moderate nausea and vomiting in 39%. BCNU toxicity included severe hematologic toxicity in 21%, including 1 death. Significant pulmonary toxicity was reported in 5 cases, including 1 death. (no Refs)

5. EXPERIENCE WITH CF-252 NEUTRON THERAPY FOR MALIGNANT GLIOMA (MEETING ABSTRACT)

Maruyama Y, Chin HW, Young AB, Bean J, Tibbs P, Beach JL
Departments of Radiation Medicine and Neurosurgery, University of Kentucky Medical Center, Lexington, KY, 40536
Am J Clin Oncol; 5(2):123 1982

We are currently studying Cf-252 interstitial neutron therapy for malignant gliomas. Neutron therapy (NT) using fast neutron beams has been on trial for approximately 10 years. Extensive trials have shown that the mean survival times following large-field irradiation of the brain using photon therapy (PT) or neutron base therapy (NBT) are the same. Autopsies of NBT-treated brain tumor patients have shown that no residual tumor is present after the NBT beam thearpy. This suggests that more localized NT may offer advantages for treatment while avoiding the toxic side effects of NBT. The basic approach has been whole-brain PT with a single interstitial im-

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plantation of Cf-252 directly into the hemispheric glioblastoma multiforme. PT dose was 6000 rad. NT dose at 1 cm was approx 1500 rem and at 2 cm was approx 500 rem. NT was generally performed before PT. We have studied the feasibility of more localized NT by means of interstitial implants using the radioisotope Cf-252 for brain tumors. NT was combined with 6000 rad of whole-brain PT. The procedures for NT, which will be described, utilize craniotomy, tumor debulking, and later applicator insertion under CT (computed tomography) guidance through burr holes into the residual tumor mass. Of 11 glioblastoma multiforme patients 5 received standard PT and 6 were treated with NT plus 6000 rad of whole-brain PT. All Cf-252 NT patients tolerated the procedures well without problems. It appears that the method can be applied in the clinic and a clinical trial is being initiated. It offers a novel form of NT for heretofore incurable malignant brain tumors. (no Refs)

6. ADVANCES IN DIAGNOSIS AND TREATMENT OF OLIGODENDROGLIOMAS OF THE BRAIN. EIGHTY-FOUR SURGICAL PATIENTS.

Paillas JE, Grisoli F, Hassoun J, Torres-Garcia T, De Laforte C
Clinique Neuro-Chirurgicale, Centre Hospitalier Universitaire de la Timone, bd Jean-Moulin, 13005 Marseille Cedex, France
Sem Hop Paris; 58(14):851-856 1982

The authors report their experience of 84 patients with oligodendroglioma seen over a 34 year period. The low incidence of these brain tumors is underlined. Oligodendroglioma is the most epileptogenic of brain tumors. The clinical picture may resemble 'essential' epilepsy. Normal EEG should be considered suspect in confirmed epileptic children and adolescents since oligodendroglioma is the most common of all tumors which induce long-standing epilepsy. Emphasis is put on the importance of computerized tomography and radionuclide scanning for early detection of these tumors. Both procedures are very helpful for deciding on the best operative approach and for determining whether the lesion is malignant or not. The authors advise tumorectomy, which should be as complete as possible, followed by systematic radiotherapy, even if histopathological criteria indicate a benign tumor. With this therapeutic regimen mean survival rates are significantly higher than those published previously. (Author abstract) (42 Refs) (In FRE)

7. EFFECT OF AGE AND REOPERATION ON SURVIVAL IN THE COMBINED MODALITY TREATMENT OF MALIGNANT ASTROCYTOMA.

Salcman M, Kaplan RS, Ducker TB, Adbo H, Montgomery E, Schold SC
Div. Neurological Surgery, Univ. Maryland Hosp., 22 South Greene St., Baltimore, MD, 21201
Neurosurgery; 10(4):454-463 1982

Study series consisted of 74 patients (43 men, 31 women: 17-85 yr old; av 47.9 yr) all of whom were assigned to a uniform multimodality treatment plan. Surgical resection was undertaken initially and was followed by 6300 rads of ionizing radiation. Prior to any treatment, patients were treated with carmustine at 100 mg/square meter/day for 3 consecutive days at 8-10 wk intervals. If initial therapy failed, all patients were then treated with Phase I agents (microwave hyperthermia, dimethyl sulfoxide (DMSO)-adriamycin, DMSO-cytoxan or azarinylbenzoquinone). Forty patients underwent a second operation with an av survival time of 37 wk. The majority of operations were carried out with the aid of the operating microscope and the carbon dioxide laser. The most important prognostic factor for survival in both reoperated and single-operated patients was age. The longer survival of patients aged 40 yr or younger was not related to tumor grade, tumor location, sex, therapy received or complications. (27 Refs)

8. FAMILIAL GLIOMAS: REPORT OF FOUR FAMILIES, WITH CHROMOSOME STUDIES.

Chadduck WM, Netsky MG, Salcman M, Bigner DD
Post Office Drawer 4666, Martinsville, VA, 24115
Neurosurgery; 10(4):445-449 1982

Eight case reports of glioma in four families are presented along with computed tomography scans and histologic results. In addition to chromosome analysis, cases were reviewed with respect to common environmental factors such as diet, atmospheric toxins or exposure to viral infections. Low grade, 'mirror' tumors were found in two brothers of one family and multiple CNS abnormalities were found in another family which suggest an inclusive genetic abnormality of the nervous system. Karyotyping studies were done on peripheral blood samples; normal chromosome numbers and patterns were found in all cases. Additional studies on chromosomal analysis of cultured tumor cells or a comparison of blood and tumor cells might yield additional information. Previous studies indicated a genetic factor in neurological disorders; one investigation disclosed seven cases of glioma among 5,262 relatives of 100 patients with glioma, while none were found among controls. The authors suggest formation of a tumor registry to report cases of familial gliomas. (14 Refs)

NEURONAL CELL AND PRIMITIVE BIPOTENTIAL PRECURSOR CELL TUMORS

9. DISEASE FACTORS THAT INFLUENCE THE PROGNOSIS OF PATIENTS WITH LOCALIZED AND REGIONAL NEUROBLASTOMA (MEETING ABSTRACT)

Evans AE, D'Angio GJ, Sather H
Children's Hospital Cancer Research Center, Philadelphia, PA
Am J Clin Oncol; 5(2):129 1982

Correct staging of patients can be an important factor in the selection of proper treatment. Neuroblastoma has a uniquely wide range of prognoses from predictably spontaneous regression to relentless progression and death. Determination of those disease variables that have significant predictive value is essential for the therapist. Staging of neuroblastoma has to date, included such factors as encapsulation, resectability, amount of residual disease, presence and site of regional lymph nodes, and sites of distant spread. To determine which factors influenced outcome in patients with regional disease, information was abstracted from the records of 257 patients entered on two CCSG (Children's Cancer Study Group) studies for localized neuroblastoma. The information analyzed included the size and extent of the primary tumor the presence of microscopic or gross residual disease, the surgeon's impression of the site, and involvement of regional nodes and their histologic appearance. The independent variables that correlated best with favorable outcome were 1) complete removal of the primary tumor, 2) unilateral disease, and 3) negative lymph nodes according to the surgeon. Bad prognostic factors were 1) tumor infiltrating across midline structures and 2) positive contralateral lymph nodes. Factors not influencing outcome were gross or microscopic residual disease. (no Refs)

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MESODERMAL TUMORS OF THE CNS

10. IMPROVED TREATMENT RESULTS AND LEUKOENCEPHALOPATHIC CHANGES IN PATIENTS WITH NEOPLASTIC MENINGITIS TREATED WITH INTRATHECAL METHOTREXATE AND THIOTEPA (MEETING ABSTRACT)

Grossman S, Ahn H, Trump D, Thompson G, Owens A
The Johns Hopkins Oncology Center, Baltimore, MD, 21205
Proc Am Soc Clin Oncol; 1:C-281 1982

The purpose of this study is to evaluate the efficacy and toxicity of combination intrathecal chemotherapy in pts with neoplastic meningitis (NM). From Jan-Dec 1980 18 pts (11 breast, 2 lymphomas, 2 leukemias, 3 other malignancies) with NM received radiotherapy to symptomatic areas of the neuroaxis and 2 or more weekly cycles of intraventricular thiotepa (10mg on day 1) and methotrexate (10mg on day 4). These pts have been followed a minimum of 330 days. Twelve of 14 (85%) cleared their CSF (cerebrospinal fluid) cytology. Eight of 10 pts who survived more than 198 days following the initiation of treatment for NM were noted to have leukoencephalopathic changes on computer axial tomographic scans (6 pts) or at autopsy (2 pts). None of these pts had clinically diagnosed leukoencephalopathy prior to these diagnostic studies. The pts who developed these leukoencephalopathic changes differed from the other pts in that they had a longer survival (351+ vs 156 days), received more intrathecal chemotherapy (15.8 vs 6.5 cycles), had more cranial radiotherapy (75% vs 50%) and were more likely to have normal CSF flow dynamics as measured by radionuclide ventriculography (4/7 vs 1/7). The response rates and length of survivals seen in this small series are superior to those previously reported for pts with NM. Treatment-related neurotoxicity will probably be more commonly recognized with the development of more effective therapeutic regimens for NM and the longer survival of these pts. (no Refs)

11. PHARMACOKINETICS OF INTRAVENTRICULAR THIO-TEPA (TT) IN PATIENTS WITH MENINGEAL CARCINOMATOSIS (MEETING ABSTRACT)

Grochow LB, Grossman S, Garrett S, Murray K, Trump D, Colvin M
The Johns Hopkins Oncology Center, Baltimore, MD, 21205
Proc Am Soc Clin Oncol; 1:C-76 1982

TT (Thio-TEPA, Triethylenethiophosphoramide) is being used in Phase III studies for the treatment of meningeal carcinomatosis although studies in primates with radiolabelled drug suggest 'that CSF would not serve as an effective route for drug delivery'. Ventricular and lumbar cerebrospinal fluid (CSF) and plasma concentrations of TT were determined in 13 patients receiving 10 mg TT by ventricular reservoir. Concentrations were determined by gas-liquid chromatography with a nitrogen-phosphorus detector after extraction with ethyl acetate using diphenylamine as an internal standard (lower level of sensitivity 0.5 ng/ml). Five to eight ventricular CSF and plasma samples and a single lumbar sample were obtained over 24-48 hours after intraventricular therapy. TT was rapidly distributed in CSF with an initial half-life of 20 mins. The subsequent exponential half-life was 8 hrs. Lumbar samples were within 50% of 'simultaneous' ventricular samples in patients without ventricular outflow block. TT plasma concentrations reached a peak 1-3 hrs, after injection and were 0.5% of CSF levels. CSF half-life was 14 hrs in patients witn ventricular outflow block vs 4 hrs in patients without obstruction. CSF concentration at 1/2 hr after injection ranged from 20-200 ug/ml. Ten hrs after injection concentrations remained above 0.1 ug/ml. Disposition of TT appears to be similar to methotrexate with potentially therapeutic concentrations maintained for hrs after injection. (no Refs)

12. MENINGEAL GLIOMATOSIS SECONDARY TO BRAIN STEM GLIOMA (MEETING ABSTRACT)

Packer RJ, Allen JC, Ghavimi F
Memorial Sloan-Kettering Cancer Center, New York, NY, 10021
Proc Am Soc Clin Oncol; 1:C-688 1982

Brain stem gliomas (BG) are locally infiltrative tumors with variable degrees of malignancy in which dissemination is considered rare. Four of 15 (27%) children with newly diagnosed BG seen consecutively over the past 40 months developed clinically significant meningeal gliomatosis (MG). Two children with MG and 4 children without MG underwent surgical exploration at time of diagnosis. No important differences in the CT (computerized tomography) appearance of the initial tumors were noted between the 2 groups. Symptoms of MG occurred at a median of 5.5 mos (range 4-8 mos) after diagnosis and in 3 children was the initial sign of disease relapse. Presenting symptoms of MG were local back pain (4), progressive paresis (3), headache (2) and bladder dysfunction (2). Myelography was performed in all children and in 3 demonstrated multifocal intradural filling defects and high degree block, suggesting subarachnoid disease. Lumbar cerebrospinal fluid (CSF) cytology was negative for malignant cells in 3 of 4 children with MG, despite the presence of a CSF pleocytosis (4 of 4) and elevated protein (3 of 4). In the one child with positive CSF cytology, myelography was normal and the extent of MG could only be appreciated at autopsy. All 4 children with MG died with a median of 3 mos (range 1 to 7 mo) following onset of MG. Necropsy confirmed diffuse MG in all 4 children. Foci of malignant astrocytoma were detected at the primary site and in areas of leptomeningeal involvement. (no Refs)

TUMORS OF THE CRANIAL AND SPINAL NERVE ROOTS

13. HEMANGIOPERICYTOMAS OF THE SPINE.

Muraszko KM, Antunes JL, Hilal SK, Michelsen WJ, Matsui T
(c/o Michelsen) 710 West 168th St., New York, NY, 10032
Neurosurgery; 10(4):473-479 1982

Four cases of hemangiopericytomas of the spine are presented. Presurgical procedures included computed tomography scans and spinal angiography, which permits delineation of the vascular supply of the tumor. Due to the highly vascular nature of the tumor, the tumors were selectively embolized by use of gelfoam, silastic or other agents administered via catheters. In two cases, the reduced vascularity allowed the gross removal of the tumors. In the third case, the tumor was too extensive and was not amenable to radical excision. Postoperative radiotherapy was employed in three of the four cases; preoperative radiotherapy decreased vascularity in one of the cases. Past experience indicates that chemotherapy has not been successful. In two patients, the postoperative course was benign; in one patient, subsequent lung metastases were found. One patient was lost to follow up. Follow up in the four cases is limited and the natural course of the tumor is unpredictable, so it is impossible to say whether a cure was achieved in any of the cases. (55 Refs)

14. ELECTRON MICROSCOPIC STUDIES OF GLANDULAR SCHWANNOMA (MEETING ABSTRACT)

Uri AK, Witzleben L
Department of Pathology, Children's Hospital of Philadelphia and University of Pennsylvania, School of Medicine Philadelphia, PA

Lab Invest; 46(1):17P 1982

Glandular schwannoma is a rare neoplasm, with only nine cases reported in the English-speaking literature. None of these previous reports have included the results of ultrastructural examination of the tumor. We have had the opportunity to study an example of this tumor by light and electron microscopy. The patient was a 15-year-old boy with neurofibromatosis, and the glandular elements were found in a retroperitoneal lesion which was predominantly neurofibrosarcoma. By light microscopy the glandular elements showed nonciliated columnar and cuboidal epithelial lining. All glands showed mucicarminophilic and diastase-resistant periodic acid-Schiff-positive material intraluminally and on cell surfaces. Although the neural part of the tumor was found to be a high grade malignant schwannoma with 40 mitoses per high power fields, the glandular component appeared to be benign. Electron microscopy of the nonglandular elements revealed features suggesting the principal constituent cells were of Schwann cell origin. Electron microscopy of the glands revealed that the lining cells themselves had numerous microvilli on their apical surface, junctional complexes, cytoplasmic electron-dense granules, and a few vesicles, as well as numerous mitochondria, abundant endoplasmic reticulum, and scattered centrioles. No mucus was seen in the cells. Glycocalyx was prominent around the microvilli, and a basement membrane underlay the epithelium. (no Refs)

SECONDARY TUMORS OF THE CNS

15. PITUITARY AND HYPOTHALAMIC METASTASES: 5 CASES.

Ozanne P, Jedynak CP, Charbonnel B, Derome PJ
Clinique Medicale B, Hotel-Dieu, F 44035 Nantes Cedex, France

Ann Med Interne (Paris); 133(2):92-96 1982

Metastases of malignant tumors to the pituitary gland were observed in five patients (3 men and 2, 40-64 yr old). The primary tumors were rectal cancer, clear-cell carcinoma of the kidney, breast cancer, epithelioma of digestive type and trabecular vesicular carcinoma of the thyroid gland. The pituitary metastasis was diagnosed or suggested by radiological examinations in three patients, while it was diagnosed at autopsy in one patient and by biopsy examination in another. The metastasis was revealed by chiasmatic syndrome in 3/5 cases and by diabetes insipidus in one. Transsphenoidal surgery was possible and successful in 3/5 cases. Literature data indicate that the frequency of pituitary metastases is 1-54%. The primary tumor having pituitary metastasis is located most frequently in the breast, lungs or stomach in women and in the lungs, prostate and urinary bladder in men. The pituitary metastases appear most often to remain unrecognized. Therefore, careful examination of the slightest signs is required in view of the therapeutic possibilities. (32 Refs) (In FRE)

OTHER THERAPY OF CNS MALIGNANCIES

16. PHASE I-II TRIAL OF INTRACAROTID (IC) CIS-DIAMMINEDICHLORO-PLATINUM (DDP) IN PATIENTS WITH INTRACEREBRAL TUMORS (ICT) (MEETING ABSTRACT)

Feun L, Wallace S, Stewart DJ, Leavens M, Savaraj N, Burgess MA, Young S, Benjamin RS
University of Texas System Cancer Center, Houston, TX, 77303

Proc Am Soc Clin Oncol; 1:C-764 1982

Twenty-two patients (pts) with intracerebral tumors progressing after radiation +/- chemotherapy have been treated with IC DDP. The internal carotid artery was temporarily cannulated using a percutaneous transfemoral approach. All pts received mannitol and IV fluids; 18 pts received Decadron 50 mg IV BID x 2 d. IC DDP, 60-120 mg/m2 in 175-250 cc normal saline with 1000 units heparin was infused over 1 hr. Courses of IA DDP were repeated monthly. Patients were evaluated by both CT (computerized tomography) scan and neurologic exam. All responding pts were receiving stable maintenance doses of steroids. Duration of response ranged from 4 (+) to 60 (+) wks in pts with malignant gliomas. Toxicity consisted of retinal toxicity (3 pts), seizures (3), motor weakness (3), gastrointestinal (10), renal (2), ototoxicity (3), ear/eye pain (3) and myelosuppression (2). Serious toxicity usually occurred at doses greater than or equal to 75 mg/m2. IC DDP appears to have activity in malignant gliomas and in pts with progressive brain metastases. (no Refs)

17. PHASE II CLINICAL TRIAL OF CIS DICHLORODIAMMINE PLATINUM (CIS DDP) IN METASTATIC BRAIN TUMORS (MEETING ABSTRACT)

Kolaric K, Roth A, Pavelic Z
Central Institute for Tumors, 41000 Zagreb, Yugoslavia

Proc Am Soc Clin Oncol; 1:C-714 1982

Thirty four consecutive untreated patients with brain metastases recorded by CAT (computerized axial tomography) scans or radionuclide scans plus neurological examinations underwent the treatment. Pathohistology of primaries has shown mainly breast (8) and lung (8) carcinomas and melanomas (10). Other localizations of primaries were infrequent. Cis DDP was administered 30 mg/m2 body surface daily, 4 days. All the patients received at least 2 cycles and 33 have been evaluated. No corticosteroids were administered concurrently. Objective response (7 complete and 7 partial remissions) was observed in 14 out of 33 patients (42%). Six stable disease cases were also noted. Complete response (4-11 + months) was observed in breast cancer (4), lung cancer (1) and melanoma (2). Seven partial responses lasted 2-5 months. Antitumor activity of Cis DDP was also noted in extracerebral tumor lesions, especially in breast cancer patients. Toxicity was moderate but tolerable. (no Refs)

18. A PHASE II TRIAL OF PRE-RADIATION CYCLOPHOSPHAMIDE IN NEWLY DIAGNOSED DISSEMINATED CHILDHOOD BRAIN TUMORS (MEETING ABSTRACT)

Allen JC, HelsonL, Jereb B
Memorial Sloan-Kettering Cancer Center, New York, NY, 10021

Proc Am Soc Clin Oncol; 1:C-689 1982

Children with disseminated primary intracranial malignancies at diagnosis have a poor prognosis following conventional radiation therapy. Once neuraxis radiation is administered it is difficult to add intensive chemotherapy. A modified phase II trial of pre-radiation chemotherapy was conducted in 14 poor risk patients. Eleven had disseminated CNS disease and 2 had bone marrow involvement at diagnosis. Their diagnoses were medulloblastoma (5), pineoblastoma (3), cerebral primitive neuroectodermal tumor (3), dysgerminoma (2) and choroid plexus carcinoma (1). Nine received 2 courses of intravenous cyclophosphamide (80 mg/kg) alone over 8 weeks and 5 others received 3 daily doses of intrathecal Ara-C (cytosine arabinoside) (50 mg/m(2)) and oral hydroxyurea (40 mg/kg) with each course of cyclophosphamide. There were 4 complete responses (2 dysgerminomas, 1 pineoblastoma, 1 primitive neuroectodermal tumor) and 4 partial responses (3 medulloblastomas, 1 pineoblastoma) to chemotherapy alone for a response rate of 57%. Twelve patients subsequently tolerated the planned dose of neuraxis radiation. The median survival of all patients was 10 months and 6 of 7 deaths were related to recurrent disease. The hematologic toxicity was appreciable and 1 death resulted from gram negative septicemia. Aseptic meningitis occurred in 4 out of the 5 patients receiving intrathecal Ara-C. (no Refs)

19. RECURRENT PRIMARY BRAIN TUMORS: HIGH DOSE BCNU AND AUTOLOGOUS BONE MARROW 'RESCUE' (MEETING ABSTRACT)

Mortimer J, Bay J, Livingston R B, Groppe CW
Cleveland Clinic Foundation, Cleveland, OH, 44106
Proc Am Soc Clin Oncol; 1:C-678 1982

In 9 patients whose primary brain tumors had progressed by computerized tomography (CT scan) and neurologically, and who had received maximal surgery and radiation therapy, BCNU (carmustine) was given over 3 days to a total dose of 1050-1200 mg/M2. Histologically, 6 originally had grade IV, 1 grade III and 2 grade II astrocytomas. In 2 of the 3 treated with 1050 mg/M2, 5 FU (5-fluorouracil) was administered simultaneously as a continuous infusion (1000 mg/M2 for 3 days). Cryopreserved autologous bone marrow was infused 24-96 hours after chemotherapy was completed. Except for one person who dies of sepsis on day 11 with pancytopenia, reconstitution was achieved hematologically in all patients with median nadir white blood cell and platelet counts on days 18 and 17, respectively. In all patients who reconstituted, absolute granulocytes exceeded 500 by day 23 and platelets exceeded 50,000 by day 25. There was no evidence of delayed myelosuppression at 4-6 weeks. Response, defined as decreased tumor mass on CT scan and decreased requirement for dexamethasone, occurred in 5/8 evaluable. Median response duration was 300 days, with 1 patient still responding at 366+ days. In addition to the septic death, complications included 1 patient with significant hepatic dysfunction (chronic), 1 with deep venous thrombosis, and 1 with symptomatic interstitial pulmonary fibrosis which promptly resolved on steroids. Nonhematopoietic side-effects were not observed in the 3 patients treated at 1050 mg/M2 of BCNU. (no Refs)

20. IMPROVED SURGICAL RESECTION OF HUMAN BRAIN TUMORS: PART 1. A PRELIMINARY STUDY.

Murray KJ
Johns Hopkins Hosp., Blalock 1404, 600 N. Wolfe St., Baltimore, MD, 21205
Surg Neurol; 17(5):316-319 1982

Twenty-three patients underwent craniotomies for brain malignancies. One hundred eleven fluorescein-stained and 75 nonstained tissue biopsies were obtained for histopathological examination using a special arc-lighting system connected to a conventional surgical headlight. Of the 75 nonstained specimens, 71 (94.7%) were negative for tumor and 4 demonstrated the presence of tumor. Ninety-four (84.7%) of the fluorescent tissues obtained were reported as having neoplasia and the remaining 17 showed characteristics consistent with necrotic tissue debris. All stained tissues obtained in this study demonstrated visible fluorescence within neoplastic tissue margins harboring abnormally permeable blood-brain barriers. (Author abstract) (11 Refs)

21. INTERSTITIAL IMPLANTATION OF BRAIN TUMOR: PRELIMINARY REPORT (MEETING ABSTRACT)

Jepson JH, Apuzzo M, Neblitt D

Divison of Radiation Oncology, City of Hope National Medical Center, Duarte, CA, 91010

Am J Clin Oncol; 5(2):124 1982

Interstitial implantation of intrinsic brain tumors using a variety of radionuclides has been employed in Europe for several decades. More recently this technique has been introduced in the United States. Among the important factors to be considered when this technique is employed are the tumor volume, its accessibility and location, the radionuclide characteristics, and the number of catheters that can be placed safely and at the same time achieve optimum geometry. In developing our present technique of multicatheter implantation in an attempt to obtain geometry, numerous technical factors have been ironed out, allowing us to achieve optimum conditions for each patient. Employing the BRW-CT stereotaxic system, it is now possible to place multiple catheters accurately within the tumor volume. A further advancement is the Apuzzo-Gutin catheter, which allows easy afterloading of radionuclides. At this writing, five patients with intrinsic brain tumors have undergone this procedure without any major complications. Two patients who had recurrence following whole-brain radiation were retreated by implanting iridium-192. Three patients were treated primarily with iridium implantation followed by whole-brain irradiation. One death occurred from nonneurological disease at 3 months. One patient died 23 months after his implant. Three patient are alive and well within a few months of this treatment. The procedure and apparatus will be discussed and the pathology described. (no Refs)

OTHER CLINICAL ASPECTS OF CNS CANCER

22. BRAIN TUMOR IMAGING BY POSITRON EMISSION COMPUTED TOMOGRAPHY USING 11C-LABELED AMINO ACIDS.

Hubner KF, Purvis JT, Mahaley SM, Robertson JT, Rogers S, Gibbs WD, King P, Partain CL

Oak Ridge Associated Univ., P.O. Box 117, Oak Ridge, TN, 37830

J Comput Assist Tomogr; 6(3):544-550 1982

We report our preliminary clinical results on positron emission tomography of human cerebral tumors with 11C-tagged amino acids. Carbon-11-DL-valine and 11C-DL-tryptophan were used for imaging the tumors. Some attempts at quantitation of the uptake were also carried out. The implications of these observations are discussed. (Author abstract) (20 Refs)

23. RETROMASTOID APPROACH FOR BIOPSY OF BRAIN STEM TUMORS.

Baghai P, Vries JK, Bechtel PC, Hoffman HJ, Reigel DH
Dept. Neurosurgery, Univ. Pittsburgh Sch. Medicine, Montefiore Hosp., Pittsburgh, PA
Neurosurgery; 10(5):574-579 1982

A technique for brain stem biopsy using the retromastoid approach is described, and results in five patients (4 brain stem gliomas, 1 medulloblastoma) are reported. After incision, a retromastoid craniectomy was performed. Then, the dura meter was opened, the cerebellum exposed, and a microsurgical self-retaining pillar-and-post retractor was used to lift the cerebellum away from the lower cranial nerves and expose the lower pons and medulla. The cerebellum was retracted inferiorly, the superior petrosal vein coagulated, and the trigeminal nerve, upper pons, and lower midbrain exposed. The ventrolateral portion of the pons between the emergence of the fifth and seventh cranial nerves is recommended as a biopsy site. A diagnostic specimen was obtained in each case. Complications were limited to mild headache, nausea, and incisional pain. Patients were usually able to ambulate on the first postoperative day and were discharged on the seventh day. This approach would be expected to cause minimal complications because all cranial nerve nuclei are far removed from the biopsy site. Proper diagnosis of brain stem lesions can affect treatment; one patient with clinical and computed tomographic evidence of brain stem glioma was found to have medulloblastoma and treatment was changed. The retromastoid approach for biopsy of brain stem tumors is safe, creates minimal morbidity, and has a high diagnostic yield. (27 Refs)

24. FINE NEEDLE ASPIRATION OF DEEP CEREBRUM: A COMPARISON BETWEEN NORMAL AND NEOPLASTIC MORPHOLOGY (MEETING ABSTRACT)

Crain BJ, Bigner SH, Johnston WW

Department of Pathology, Duke University Medical School, Durham, NC

Acta Cytol (Baltimore); 25(6):719 1981

Proper interpretation of thin needle aspiration biopsies of deep-seated cerebral lesions requires familiarity with normal morphologic structures as well as with neoplastic and nonneoplastic conditions that involve this region. We compared 22-gauge needle aspirates of deep white matter, basal ganglia, and thalamus from autopsies of three neurologically normal adult males with eight aspirates from tumors that occur in this location. Smears and Millipore filter preparations of needle washings were fixed in 95% ethanol and stained by the Papanicolaou method. Normal white matter contained oligodendroglia with small, dark, round nuclei and astrocytes with larger, bland, oval nuclei and occasional cytoplasmic extensions. In comparison, nuclei of astrocytomas were more variable in size and shape, with prominent elongated cytoplasmic processes producing a markedly fibrillar background. Glioblastoma multiforme was more cellular, with irregular or clefted nuclei, inconspicuous nucleoli and sparse cytoplasmic processes. Basal ganglia and thalamus consisted largely of neurons with large nuclei and prominent nucleoli. Although individual neurons were alarming, sparse cellularity distinguished these normal tissues from malignant gliomas and metastatic tumors. (no Refs)

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NEUROGLIAL CELL TUMORS

1. RADIATION TOLERANCE OF THE SPINAL CORD PREVIOUSLY-DAMAGED BY TUMOR AND OPERATION: LONG TERM NEUROLOGICAL IMPROVEMENT AND TIME-DOSE-VOLUME RELATIONSHIPS AFTER IRRADIATION OF INTRASPINAL GLIOMAS.

Kopelson G
Dept. Radiation Oncology, Salem Hosp., 81 Highland Ave., Salem, MA, 01970

Int J Radiat Oncol Biol Phys; 8(5):925-929 1982

Long-term neurological functioning was reviewed in 19 patients (11 males, 8 females, 6-69 yr old) with intraspinal gliomas who received irradiation, and doses approaching or equalling spinal cord tolerance which may be safely given to patients without an increased risk of radiation myelopathy were determined. For the 19 patients analyzed, detailed neurological examinations were reviewed immediately prior to initiation of irradiation, the subsequent neurological course, and the most recent follow-up status. The general clinical characteristics and management are presented. The majority of pre-irradiation neurological deficits returned to normal permanently post-irra-

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diation. The major cause of post-irradiation neurological deterioration was tumor recurrence. No patient demonstrated any evidence of chronic radiation myelopathy; each patient survived past the peak time-period incidence of radiation myelopathy. Long-term normal neurological functioning was achieved for many patients. When the doses for the patients were converted into fractionation regimens which emphasized fraction number, even patients whose spinal cord doses equalled, approached, or exceeded spinal cord tolerance did not demonstrate radiation myelopathy. When using the ED scheme, two patients who exceeded standard tolerance and four patients who exceeded the lower tolerance level did not develop myelopathy. (14 Refs)

2. GLIOMEDULLOMYOBLASTOMA: A CONTRIBUTION TO THE MORPHOLOGY AND BIOLOGICAL BEHAVIOR OF MYOGENIC BRAIN TUMORS.

Warzok R, Janisch W, Schreiber D
Pathologisches Institut, Ernst-Moritz-Arndt-Universitat, Friedrich-Loeffler-Strasse 23e, DDR-2200 Greifswald, E. Germany
Zentralbl Allg Pathol; 126(1/2):5-15 1982

On the basis of one observation and 38 cases found in the literature problems of histogenesis, classification and biological behavior of myogenic brain tumors and mixed neoplasms with myogenic elements are discussed. In a 2-yr-old boy, 2 mo after first clinical symptoms, a tumor of the walls of the fourth ventricle had been removed. The growth showed a large variety of histological structures. Irregularly arranged bundles of long muscle fibers with centrally located nuclei and cross striation were the most striking feature. Large cells with prominent nucleoli resembling ganglion cells were identified electron microscopically as rhabdomyoblasts. Other areas were composed of astrocytic elements or of honeycomb-like structures usually observed in oligodendrogliomas. In serial sections small cells with dark nuclei typical for medulloblastomas were found in small areas. The body died 15 mo after the onset of symptoms. The autopsy revealed a relapse in midline structures of the cerebellum. The histological picture differed substantially from that of the primary neoplasm. It was composed only of small cells, showed a large number of collagenous fibers and corresponded to a demoblastic medulloblastoma. The histological variety is regarded as an expression of the pluripotency of neoplastic elements, which are evidently capable to form neuroectodermal as well as mesenchymal structures. It is emphasized that an overgrowth of more anaplastic cells led to the described morphological changes. Gliomedullomyoblastoma is regarded as a special variant of medulloblastoma with an unfavorable prognosis. (Author abstract) (52 Refs) (In GER)

NEURONAL CELL AND PRIMITIVE BIPOTENTIAL PRECURSOR CELL TUMORS

3. INDUCTION OF NEUROBLASTOMA MATURATION BY A NEW CHEMOTHERAPY PROTOCOL.

Raaf JH, Cangir A, Luna M
Dept. Surgery, Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
Med Pediatr Oncol; 10(3):275-282 1982

Five patients, 1.5 to 9 yr old, were treated at M. D. Anderson Hospital for Stage III or IV neuroblastoma. Each was entered into a chemotherapy protocol which included cyclophosphamide, vincristine, 5-trifluoromethyl-2'-deoxyuridine (F3TdR), and papaverine, and each responded with marked reduction in size of the abdominal tumor mass. All patients then underwent exploratory laparotomy and resection or biopsy of residual tumor. In three cases, histological examination of the treated tumor showed ganglioneuroblastoma with predominance of mature cells; one patient had a mature ganglioneuroma, whereas only necrotic tissue was obtained from the fifth patient. These findings support the hypothesis that this chemotherapy protocol can induce neuroblastoma maturation. (Author abstract) (8 Refs)

4. HIGH LEVELS OF IMMUNOREACTIVE NERVOUS SYSTEM-SPECIFIC ENOLASE SERA OF PATIENTS WITH NEUROBLASTOMA.

Ishiguro Y, Kato K, Shimizu A, Ito T, Nagaya M
Dept. Biochemistry, Inst. for Developmental Res., Aichi Prefectural Colony, Kamiya, Kasugai, Aichi 480-03, Japan
Clin Chim Acta; 121(2):173-180 1982

A sensitive determination of serum nervous system-specific enolase (NSE) using an enzyme immunoassay system is described and increased NSE levels in patients with neuroblastoma are reported. The assay of human NSE was carried out with a sandwich enzyme immunoassay system for rat NSE using cross reactivity of human gamma subunit to the antibody to rat gamma subunit. Infant control samples were sera from 20 patients (15 males, 5 females, 1-7 yr old) without disease. Adult control samples were obtained from 20 healthy individuals (10 males, 10 females, 20-40 yr old). Serum samples with neuroblastoma were obtained from patients undergoing treatment. Clinical data on the patients examined are presented. Standard curves of rat (RGG) and human gamma gamma (HGG) enolases and the cross-reactivities of other forms of human enolase are presented. The reactivity of HGG enolase of the assay was approx 30% that of RGG, when assessed by comparing the amounts of HGG and RGG required to display a fluorescence intensity of 50% bound beta-D-galactosidase activity. When serum samples from normal individuals and patients with neuroblastoma were subjected to the assay after various dilutions with buffer G, almost parallel curve slopes were observed. These results indicated that the serum levels of NSE could be determined with the applied immunoassay. NSE levels in serum with neuroblastoma ranged from 13.6-330 nanog (ng)/ml (mean 96 ng/ml) which was approx 30-and 20-fold higher than that in the adult and infant control levels, respectively. NSE levels in serum with ganglioneuroblastoma were near the normal ranges. Results suggested that NSE in serum might be a useful marker for screening and therapeutic monitoring of neuroblastoma. (17 Refs)

MESODERMAL TUMORS OF THE CNS

5. CYTOLOGICAL AND CYTOGENETICAL STUDIES ON HUMAN MENINGIOMA.

Zang KD
Inst. Human Genetics, Univ. Saar, 6650 Homburg, W. Germany
Cancer Genet Cytogenet; 6(3):249-274 1982

Characteristics of meningiomas which make them a model system for the study of human cancer development are described. Meningiomas show a remarkably good correlation between karyotype and histological and growth patterns which particle cultures of the individual tumors develop in vitro.

Histological classification of meningiomas is described. In contrast to true brain tumors, meningiomas occur most offten in the fifth and sixth decade of the life and occur twice as frequently in females as in males. Characterization of meningiomas according to their respective karyotype shows a highly significant shift in sex distribution. In tumors with normal karyotypes, the male:female sex ratio is 1:3 while in more aberrant forms the ratio is approx 1:1. Chromosomal indications for virus involvement in the etiology of meningiomas are presented along with immunofluorescence data, induction of virus particles, and demonstration of episomal Simian virus 40 (SV40) DNA in meningiomas. Experimental transformation of meningioma cell cultures and fibroblast cultures of the same patients with SV40 is described. (62 Refs)

6. HYPEROSTOSING MENINGIOMAS OF THE SPHENOID RIDGE - CLINICAL FEATURES, SURGICAL THERAPY, AND LONG-TERM OBSERVATIONS: REVIEW OF 49 CASES.

Pompili A, Derome PJ, Visot A, Guiot G
Dept. Neurosurgery, Istituto Regina Elena, Viale Regina Elena 291, 00161 Roma, Italy
Surg Neurol; 17(6):411-416 1982

Thirty-three patients with en plaque, 9 with en masse (but with extensive bone involvement), and 7 with recurrent hyperostosing meningiomas of the sphenoid ridge were operated on. All patients underwent large extradural resection of the base of the skull as well as extirpation of the intradural tumors or adjacent plaques. The periorbita was involved in 13 patients (26.5%). Seventeen patients (34.7%) needed reconstruction of the base of the skull. This was achieved with autogenous bone grafts. In all but three patients, invasion of the bone by meningiomatous tissue was demonstrated histologically. Operative mortality was 4%. Total removal was possible in 91% of the patients with meningiomas located at the pterion or middle third of the sphenoid ridge. More difficult was the total removal of meningiomas of the inner third or of the entire sphenoid ridge (47%). However, long-term results have proved to be satisfying. Early surgical therapy should always be considered as the treatment of choice for such meningiomas. (Author abstract) (11 Refs)

TUMORS OF THE CRANIAL AND SPINAL NERVE ROOTS

7. SPINAL TUMORS.

Kinzl L, Burri C
Abteilung fur Unfallchirurgie, Plastische- und, Wiederherstellungschirurgie, Departement fur Chirurgie Universitat Ulm/Donau, Steinhovelstrasse 9, D-7900 Ulm/Donau, W. Germany
Chirurg; 53(5):286-291 1982

Vertebral tumors account for 2% of all skeletal tumors. Certain types of tumor, such as osteoblastoma, plasmocytoma, and eosinophilic granuloma, occur preferentially in the spinal column. Initial symptoms are usually nonspecific. Symptoms are related to the instability of the spinal column and to neurological effects produced by pressure on nerves. Spinal tumors may produce peripheral paralysis or cross-sectional syndrome, depending on the localization, aggressiveness, and direction of extension of the tumor. Spinal metastases usually present no serious diagnostic problems, since the primary tumor is usually known. Although a specific hematological indicator has been found only for plasmocytoma, various hematological parameters can be used to differentiate neoplasms from inflammatory conditions. Diagnostic methods include x-rays, computer tomography, and nuclear scintigraphy. Noninvasive methods tend to be nonspecific; biopsy is generally required for differential diagnosis. Surgery should be aimed at radical resection of tumor, decompression of the nervous system, and stabilization of the spinal column. The standard approach is ventral. The dorsal approach should be used only when the patient's condition and prognosis are poor. Individual cases may require a combined approach. Stabilization may be accomplished by various methods using bone cement and metal plates. A simple method uses a telescopic screw device. Of 29 patients with incomplete preoperative paralysis who underwent spinal fusion surgery, 17 achieved significant remission and 10 achieved complete relief from neurological symptoms; only 2 showed deterioration. (11 Refs) (In GER)

8. VISUAL EVOKED POTENTIALS IN CHIASMAL GLIOMAS IN FOUR ADULTS.

Kupersmith MJ, Siegel IM, Carr RE, Ransohoff J, Flamm E, Shakin E

Dept. Ophthalmology, New York Univ. Medical Center, New York, NY

Arch Neurol; 38(6):362-365 1981

The cases of four patients with surgically observed optic chiasm gliomas that could not be definitively diagnosed by preoperative neuro-ophthalmological or neuroradiological evaluation are described. Three patients with pituitary tumors and comparable Snellen acuity were also studied. Electrodiagnostic investigation of the glioma patients showed absent or severely attenuated pattern visual evoked potentials (VEPs) in the presence of relatively preserved Snellen acuity. Glioma of the chiasm appears to have a more profound effect on VEPs than do extrinsic compressive lesions of the anterior visual pathway, suggesting that the visual stimuli test may be useful as a noninvasive diagnostic procedure to supplement neuroradiological and neuro-ophthalmological evaluation. (17 Refs)

TUMORS OF THE CHOROID PLEXUS AND PINEAL REGIONS

9. SURGICAL MANAGEMENT OF PINEAL AREA TUMORS IN EARLY CHILDHOOD.

Demakas JJ, Sonntag VK, Kaplan AM, Kelley JJ, Waggener JD

(c/o Sonntag) 222 West Thomas Road, Phoenix, AZ, 85013

Surg Neurol; 17(6):435-440 1982

Three cases of tumors of the pineal area in young children are presented. Surgical intervention is advocated because of the greater than 50% chance of the tumor's being benign in this age group and the greater risk from radiation to the developing brain. (Author abstract) (29 Refs)

SECONDARY TUMORS OF THE CNS

10. REGIONS OF LOW DENSITY IN THE CONTRAST-ENHANCED PITUITARY GLAND: NORMAL AND PATHOLOGIC PROCESSES.

Chambers EF, Turski PA, LaMasters D, Newton TH
Dept. Radiology, Univ. California Sch. Medicine, San Francisco, CA, 94143
Radiology; 144(1):109-113 1982

The incidence of low-density regions in the contrast-enhanced pituitary gland and the possible causes of these regions were investigated by a retrospective review of computed tomographic (CT) scans of the head in 50 patients and autopsy specimens of the pituitary in 100 other patients. It was found that focal areas of low density within the contrast-enhanced pituitary gland can be caused by various normal and pathologic conditions such as pituitary microadenomas, pars intermedia cysts, foci of metastasis, infarcts, epidermoid cysts, and abscesses. Although most focal low-density regions probably represent pituitary microadenomas, careful clinical correlation is needed to establish a diagnosis. (Author abstract) (19 Refs)

OTHER THERAPY OF CNS MALIGNANCIES

11. 'THIRD SPACE' IN THE CEREBELLAR REGION AS A CAUSE OF SYSTEMIC ADVERSE EFFECTS AFTER INTRATHECAL METHOTREXATE THERAPY (MEETING ABSTRACT).

Schalhorn A, Wagner H, Wilmanns W, Stupp-Poutot G
Medizinische Klinik III im Klinikum Grosshadern der Universitat Munchen, Munchen, W. Germany
Onkologie; 4(5):268 1981

A patient with meningiosis carcinomatosa complicating carcinoma of the breast was found to have a greatly delayed fall in serum MTX levels after each of 3 divided doses of 15 mg of methotrexate (MTX), respectively, given as intralumbar injections over a 9 day period which remained at 10-7M 18 hr later and 5x10-8M after 48 hr. The cause of the abnormal pharmacokinetics was a 'third space' in the brain region. After an earlier operation on a cerebellar metastasis it was possible for MTX to be released from a large defect cavity, as from a reservoir, delayed over a longer period of time and lead to toxic side effects as a result of prolonged elevated serum levels of MTX. Even though the intrathecal MTX therapy was administered as monotherapy, after the third injection severe mucosal ulcerations and prolonged leukocytopenia and thrombopenia developed. As a consequence of these results intrathecal MTX therapy in the presence of larger tissue defects, eg, following surgery on brain metastases, hence in the presence of a cerebral 'third space', requires particularly attentive clinical and laboratory surveillance. In these cases, as well as following intrathecal administration of MTX, regular determinations of serum MTX concentrations appears necessary to ensure safe treatment. (no Refs) (In GER)

12. THE CO2 LASER IN NEUROSURGERY.

Heppner F, Ascher PW
Univ. Clinic of Neurosurgery, Graz, Austria
Int Adv Surg Oncol; 5:385-396 1982

The effects of the CO2 laser on cerebral tissue and laser treatment of lesions of the central and peripheral nervous system are discussed. Samples of human brain tissue that had been subjected to laser beams during therapy were subsequently taken and histologically examined. The effects of laser beam depends on three factors: the power output, the density of the beam (within or outside the focal plane), and the exposition time. Four-hundred and forty-five patients with lesions of CNS and peripheral nervous system were successfully subjected to surgery by the laser. By laser it took twice as long to incise skin, four times as long to cut the bone, and an equal time to split the dura compared with conventional means. However, less hemorrhage was observed. Astrocytomas, meningiomas, glioblastomas, cystic growth, epileptics, brain stem and spinal cord, and amputation stump neuromas were treated with the laser. In those patients in which the skin was also incised by laser a marked difference was observed between the scalp and the skin in the dorsal region. The scalp wounds healed quickly, whereas in the back the stitches had to be left in place twice as long as scalpel incision. Results indicated that the CO2 laser is well suited for dissection of tough gliomas and capsules of tumors. The possibility of accurately determining the depth of penetration of the pulsed laser permits the removal of tumors of the brain stem. The vaporization of the brain wound surface after extirpation of glioblastomas does not appear to influence decisively the rate of recurrence. (17 Refs)

13. CHEMOTHERAPY WITH VINCRISTINE AND BCNU/CCNU IN BRAIN TUMORS OF CHILDREN.

Metz O, Dorffel W, Gohler I, Hassler A, Mateev J, Reddemann H, Todt H, Zastrow J

Universitatskinderklinik (Carl-Zeiss-Stiftung), Kochstrasse 2, DDR-6900 Jena, E. Germany

Dtsch Gesundheitswes; 37(13):595-600 1982

A total of 21 children aged between 1 8/12 and 17 7/12 taken ill with brain tumors (11 medulloblastomas, 6 ependymoblastomas, 4 astrocytomas) were given irradiation therapy and cytostatic medication after surgery. All children covered by the study were afflicted with primary tumors and there were no signs of metastases in the cerebrospinal fluid before surgery. Drainage operations were regarded as an exclusion criterion in the study. The cytostatic therapy consisted of Vincristine alone during irradiation treatment, followed by massive doses of Vincristine and carmustine (BCNU) or lomustine (CCNU) every 4 weeks. The total duration of the therapy was 1 yr. Of the 21 children, 13 (61.9%) suffered a relapse after an av of 28.3 mo (8-50 mo). Of these, eight patients died after 13-57 mo (on av after 32.4 mo) of illness. These results failed to meet the hopes pinned on postoperative irradiation and medication therapy. One of the reasons for this is probably the fact that liquor irradiation treatment was not always given consistently. No differences were observed between BCNU therapy (10 patients) and CCNU therapy (11 patients). Cytostatic medication with nitrosourea derivatives BCNU and CCNU was tolerated by the children without serious complications. In future the working group 'Pediatric Hematology and Oncology' should try to improve and maintain with consistency the therapeutic conception for treating brain tumors in children, which provides for intensive cytostatic therapy followed by irradiation after surgery. (Author abstract) (12 Refs) (In GER)

OTHER CLINICAL ASPECTS OF CNS CANCER

14. CYTOLOGICAL FINDINGS FROM CEREBROSPINAL FLUID IN CHILDREN WITH INTRACRANIAL TUMORS.

Doll R, Neumarker KJ, Krause H, Arndt S

(c/o Neumarker), Abteilung fur Kinderneuropsychiatrie der Nervenklinik (Charite), Schumannstrasse 20/21, DDR-1040 Berlin, E. Germany

Dtsch Gesundheitswes; 37(2):63-66 1982

To evaluate the informative value of studying the cerebrospinal fluid in children with intracranial tumors, fluid was obtained preoperatively by lumbar puncture from 86 children. The study group included 19% malignant, 64% benign and 17% unclassified tumors. Studies were most productive, with pathological findings in 39% of patients, with intracranial tumors. Cytological studies were a strong point, providing the most frequent pathological findings. Pleocytosis was found in 39% of children, most frequently associated with medulloblastomas. Tumor cells were found in the cellular sediment of cerebrospinal tumors. Most of the cellular sediments showed an increase in granulocytes, characterized in 45% of patients by eosinophilic granulocytes and in 13% by neutrophilic granulocytes. Immunocompetent cells were found in 33% of the differential sediments, particularly with malignant tumors. (18 Refs) (In GER)

15. PRIMARY BRAIN STEM TUMOURS.

Strange P, Wohlert L

Dept. Neurology, Rigshospitalet, Copenhagen, Denmark

Acta Neurochir (Wien); 62(3/4):219-232 1982

The material consisted of 31 patients with primary brain stem tumors who were investigated retrospectively. Twenty patients were younger than 16 yr of age (range: 1 1/2-65 yr). The mean age was 11 yr. The female/male sex ratio was 19/21. Histological diagnoses were available for 18 patients. All of the verified tumors were gliomas. The diagnoses in 12 cases were made by section or biopsy; in 15 by standard clinical and radiological examinations and in 4 by exploratory operations. Headaches, mental changes, speech and gait disturbances were the most common symptoms at the onset of the illness and at the time of diagnosis. The mean latency period between the emergence of symptom(s) until diagnosis was 4 mo (range: 1/2-48 mo). Amongst the dominant objective findings were failure of the V, VI and VII cranial nerves, pyramidal tract symptoms, ataxia and nystagmus, occurring singly or in combination. Pneumoencephalograms disclosed characteristic changes in 25 patients (83%). Fourteen patients (45%) received radiation treatment, from which 5 (36%) obtained a temporary remission in their symptoms. The postdiagnostic mean survival period for the patients was 15 mo (range: 0-92 mo). The survival time was found to depend on the number of damaged cranial nerve nuclei at the time of diagnosis and on the degree of severity and duration of the accompanying hydrocephalus. The prognosis was unfavorable, as the percentage of patients who survived for 2 yr was only 6%, and a total duration of illness longer than 2 yr occurred in only seven patients. None of the patients were still surviving at the conclusion of this investigation. (Author abstract) (11 Refs)

16. BRAIN TUMOR EVALUATION USING RB-82 AND POSITRON EMISSION TOMOGRAPHY.

Yen CK, Yano Y, Budinger TF, Friedland RP, Derenzo SE, Huesman RH, O'Brien HA

(c/o Budinger) Donner Lab., Room 230, Univ. California, Berkeley, CA, 94720

J Nucl Med; 23(6):532-537 1982

Positron emission tomography of the brain with 75-sec rubidium-82 obtained from a portable generator (25-day Sr-82 to Rb-82) was used to evaluate the integrity of the blood-brain barrier (BBB) in patients with brain tumors. Rubidium is normally excluded from the central nervous system by the intact BBB, but when the BBB is disrupted by a tumor, Rb enters and pools in the extravascular spaces of the central nervous system. Since Rb is also rapidly cleared from the blood, a high tissue-to-blood ratio of the Rb-82 tracer is achieved in regions of BBB disruption after intravenous injection. With dynamic positron emission tomographic imaging, the extravasation of the Rb tracer can be evaluated independent of the intravascular Rb concentration, and very small changes in the BBB permeability can be detected. These results of our studies in eight patients show that this technique is a promising method for evaluation of the BBB integrity in brain-tumor patients. (Author abstract) (21 Refs)

SELECTED PRECLINICAL ASPECTS OF CNS CANCER

17. MONOCLONAL ANTIBODIES DEFINING MARKERS WITH APPARENT SELECTIVITY FOR PARTICULAR HAEMOPOIETIC CELL TYPES MAY ALSO DETECT ANTIGENS ON CELLS OF NEURAL CREST ORIGIN.

Kemshead JT, Fritschy J, Asser U, Sutherland R, Greaves MF

Membrane Immunology Lab., Imperial Cancer Res. Fund, Lincoln's Inn Fields, London WC2A 3PX, England

Hybridoma; 1(2):109-123 1982

Monoclonal antibodies (MAs) were raised against either hemopoietic or neuronal cells, and the extent of sharing of selective expression in different tissue systems was studied. Biochemical data confirmed some of the serological results. Four antigens defined as being present on a subset of hemopoietic cells were also shared with cells of neural crest origin. For example, one MA reacting preferentially with immature (B) lymphoid cells and their corresponding leukemias also bound neuroblastoma, melanoma, and retinoblastoma cell lines. No binding to astrocytoma or medulloblastoma cultured cells was detected by indirect immunofluorescence, however. Other MAs binding hemopoietic cells showed no detectable binding to any neural crest derived cell line. MAs raised against either neuroblastoma cells or human fetal brain produced probes for antigens unique to neural crest cells and for antigens shared with cells in the hemopoietic system. One line, UJ 308, reacted with cells of the myeloid lineage as well as neuroblastoma cells. One antigen on neuroblastoma cells, a 'thymic cortex' 45,000-49,000 mol wt antigen associated with the 12,000 mol wt beta2-like molecule, may be a gene product of the major histocompatibility complex. The extent of cross-reactivity of the present study could be much greater than found between only hemopoietic and neural cells. Nevertheless, the reagents may still be useful for identifying subsets of cells within a population. (41 Refs)

18. ALKALINE PHOSPHATASE ACTIVITY IN CULTURED MENINGIOMA CELLS.

Takahara N, Herz F, Hirano A
(c/o Herz) Div. Neuropathology, Montefiore Hosp. and Medical Center, 111 East 210th St., Bronx, NY, 10467
Acta Neuropathol (Berl); 57(1):45-50 1982

The production and modulation of alkaline phosphatase (AP) activity in cultured meningioma cells is described. AP activity in cultured meningioma cells is described. AP activity varied over a wide range and did not correlate with the histological type of meningioma from which the cultures were derived. AP activity appeared to be independent of the number of transfers of a given culture. Acid phosphatase levels showed little variation among the different cultures. Similarly to brain and to human intracranial tumors, meningioma cells produced a heat-labile AP corresponding to the liver/bone/kidney isozyme. Both glucocorticoids and sodium butyrate, which elicit significant increases in AP activity in cultures derived from a variety of primary and metastatic tumors of the CNS, were found to cause only a slight increase in activity in cultured meningioma cells. Hyperosmolar growth conditions which stimulate AP activity in many continuous human tumor cell lines such as HeLa S3, C41, and HT-29 but not in cultures derived from intracranial tumors, were effective inducers of AP activity in the meningioma cells. (36 Refs)

19. ENOLASE ISOENZYME DISTRIBUTION IN THE HUMAN BRAIN AND ITS TUMOURS.

Royds JA, Parsons MA, Taylor CB, Timperley WR
Dept. Biochemistry, Univ. Sheffield, Sheffield, England
J Pathol; 137(1):37-49 1982

Distribution of alpha, beta, and gamma enolase subtypes in the human brain was studied and the data were extended to the study of CNS neoplasms. Results showed that the enolase isoenzyme composition of the tumor is similar to that of cell type from which the tumor is derived. Thus, astrocytomass, ependymomas, and meningiomas contain high levels of alpha enolase; acoustic neuromas showed strong staining for alpha enolase within the long spindle-shaped neurilemmal cells of the Antoni type A tissue, whereas cells of Antoni type B tissue showed weaker staining. (22 Refs)

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NEUROGLIAL CELL TUMORS

1. INFANTILE SMALL CELL GLIOMAS.

Friede RL, Janzer RC, Roessmann U
Dept. Neuropathology, Univ. Gottingen, Robert-Koch-Strasse 40, D-3400 Gottingen, W. Germany
Acta Neuropathol (Berl); 57(2/3):103-110 1982

Fourteen juvenile patients (6 male, 8 female) with small cell gliomas were studied in two institutions on two continents. The age at onset of symptoms varied from 10.5 mo to 20 yr, av 9 yr. Interval between onset of symptoms and diagnostic intervention (when done) was 3 wk to 15 mo (av 5 mo). Presenting symptoms depended upon anatomic localization. Most tumors arose in the diencephalon or brain stem and were composed of a poorly differentiated small cell component having a pronounced tendency to differentiate into a glioma. The tumors spread easily throughout the CNS. Electron microscopy revealed signs of neuroblastic differentiation. One surgically treated patient was not available for follow-up. One patient was still alive 15 mo after surgery without apparent recurrence. The other patients died within 1 yr of surgical intervention. Longest survival between onset of symptoms and death was 21 mo in a patient who had not undergone surgery. The

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designation 'infantile small cell glioma' overlaps both the 'metastasizing gliomas in young subjects' of Eade and Urich, and with the primitive neuroectodermal tumor of infancy of Hart and Earle. (13 Refs)

2. INTRAMEDULLARY SPINAL CORD ASTROCYTOMA VERSUS GLIOBLASTOMA. THE PROGNOSTIC IMPORTANCE OF HISTOLOGIC GRADE.

Kopelson G, Linggood RM

Dept. Radiation Oncology, Salem Hosp., 81 Highland Ave., Salem, MA, 01970

Cancer; 50(4):732-735 1982

Fourteen patients with intramedullary spinal cord astrocytoma (Grades I, II) or glioblastoma (Grades III, IV) were seen at a major referral center over a 19-yr period. Although similar surgical and radiotherapeutic techniques were used for each group, the nine patients with astrocytoma had a 5-yr actuarial survival rate of 89% with five patients alive and well at least 5 yr after treatment; none of the five patients with glioblastoma survived past 3 yr. Histologic grade is the most important factor affecting prognosis for patients with intramedullary spinal cord astrocytomas or glioblastomas, and long-term survival can be achieved postirradiation for many patients with astrocytomas with improved neurologic functioning in most. (Author abstract) (27 Refs)

3. LIMITATIONS OF HIGH DOSE INTRA-ARTERIAL 1,2-BIS(2-CHLOROETHYL)-1-NITROSOUREA (BCNU) CHEMOTHERAPY FOR MALIGNANT GLIOMAS.

Kapp J, Vance R, Parker JL, Smith RR, Mahaley MS, Neuwelt EA

Dept. Neurosurgery, Univ. Mississippi Medical Center, 2500 N. State St., Jackson, MS, 39216

Neurosurgery; 10(6,part1):715-719 1982

Limitations on the use of intracarotid infusion (ICI) of 1,2-bis(2-chloroethyl)-1-nitrosourea (BCNU) were indicated by experience in two patients with gliomas. Patient 1 was a 63-yr-old man who presented with seizures and impairment of memory. Patient 2 was a 57-yr-old woman with a 4-mo history of headache and focal left body seizures, left homonymous hemianopia and left hemiparesis. Patient 1 developed patchy necrosis of the white matter of the left hemisphere after a cumulative dose of 700 mg/square meter (m2) by left ICI at 6-wk intervals. The first occurrence of his deficit began after the third ICI and progressed to massive edema of the left hemisphere and death. Compete radiographic regression of the tumor had been noted. Patient 2 developed blindness in the eye ipsilateral to the infused carotid artery, which was first noted 8 wk after ICI of 250 mg/m2 BCNU. While her left hemiparesis improved dramatically, she returned to the hospital after 8 wk with headache and increased lethargy. A computed tomographic scan showed extension of the tumor outside the infused area, with an enhancing mass in the anterior corpus callosum and a second mass in the fourth ventricle. Various modifications in technique are proposed to deal with the problems found in these patients. (11 Refs)

NEURONAL CELL AND PRIMITIVE BIPOTENTIAL PRECURSOR CELL TUMORS

4. MEDULLOBLASTOMAS.

Choux M, Lena G, Alfonsi S, Bernard J, Pinsard N, Rigaud F, Clement R, Elbaze F, Gambarelli D, Raybaud C, Ruffo M, Hassoun J, Lerpiniere J, Lucas C, Raybaud C, Tapounie E
C.H.U. La Timone, Marseille, France
Neurochirurgie; 28(Suppl1):229pp. 1982

A report on 113 series (6,024 cases) of medulloblastomas (MDB) based on literature data is presented. MDB accounts for 3.74% of all tumors of the CNS. MDB are most commonly found in pediatric cases (74.6%), particularly in children under 5 yr (36.9%) with a major peak at 6 yr. In 66.10% of cases, MDB are located in the midline when they are found in the posterior fossa. MDB may either be circumscribed or disseminated, and cystic change is not uncommon. Neuroradiological investigations are essential in the diagnosis of MDB. Computed tomography scanning is the basic procedure for the evaluation of the intracranial lesion in more than 90% of the cases, with an exact evaluation of the tumor location in 75% of the cases. Treatment of MDB includes surgical biopsy, palliative operations, and tumor resection. Radiotherapy of MDB is based on the radiosensitivity of in vivo tumors even though in vitro results have not been verified. Less favorable prognoses are found in younger children, in girls, and in patients with hemorrhagic MDB, large tumors, midline tumors, or brain stem involvement. Total tumor resection is a favorable prognostic factor especially in children. (756 Refs) (In FRE)

MESODERMAL TUMORS OF THE CNS

5. CYSTIC MENINGIOMAS: A CLINICORADIOLOGICAL STUDY.

Dell S, Ganti SR, Seinberger A, McMurtry J
Dept. Neurosurgery, Tufts-New England Medical Center, 171 Harrison Ave., Boston, MA, 02111
J Neurosurg; 57(1):8-13 1982

A group of eight cystic meningiomas is considered, with particular reference to preoperative radiological evaluation. Computerized tomography (CT) scanning alone is inadequate for diagnosis, and the authors offer an assessment of the current methods for preoperative identification of cystic supratentorial tumors, while reviewing the multiple etiologies suggested for the CT appearance. No single process explains all the aspects of peri- or intratumoral cyst formation in meningiomas. (Author abstract) (57 Refs)

6. PRIMARY ORBITAL MENINGIOMA: A REVIEW OF 41 PATIENTS INVESTIGATED RADIOLOGICALLY.

Lloyd GA
Moorfields Eye Hosp., City Road, London, England
Clin Radiol; 33(2):181-187 1982

The x-ray features in 41 patients with histologically verified primary meningiomas in the orbit are reviewed. These tumors arise from the sheath of the optic nerve (78%) or extradurally within the orbit, remote from the nerve (22%). Sheath meningiomas occur predominantly in middle-aged women. Characteristically they give little sign of their presence on plain x-rays, but may show minor variations in the size of the optic

canal (22%) or calcification in the tumor (12.5%). The radiological diagnosis is based upon the computed tomography (CT) findings. Visual deterioration in a middle-aged or elderly patient with obvious optic nerve enlargement on CT and minimal or no enlargement of the optic canal is virtually diagnostic of a sheath meningioma. Primary extradural meningiomas in the orbit usually present with proptosis before compressing the optic nerve. The majority of these show some plain x-ray evidence of their presence such as localized or generalized orbital enlargement, hyperostosis of the orbital walls, or changes in the adjacent sinuses. In this group the tumor may be located inside or outside the rectus muscle cone and the CT changes are usually non-specific. (Author abstract) (14 Refs)

SECONDARY TUMORS OF THE CNS

7. HYPERPROLACTINAEMIA IN MALES WITH AND WITHOUT PITUITARY MACROADENOMAS.

Spark RF, Willis CA, O'Reilly G, Ransil BJ, Bergland R
Steroid Res. Lab., Beth Israel Hosp., 330 Brookline Ave., Boston, MA, 02215
Lancet; 2(8290):129-132 1982

To ascertain whether in hyperprolactinemic men pituitary macroadenomas represent the end stage of a disease process wherein the only early symptom is impotence, the features of 16 hyperprolactinemic men with radiological evidence of pituitary macroadenomas were compared with those of 10 hyperprolactinemic men without pituitary macroadenomas. All were impotent and 25 had low serum testosterone levels. The group with pituitary macroadenoma was older (48.1 vs 63.2 yr) and had tolerated impotence for longer (10.4 +-6.0 vs 4.5 +-2.1 yr). Six of them had visual field defects (none in the other group), 14 had hypopituitarism (1 in the other group), and 14 were initially seen for problems other than sexual dysfunction (whereas all 10 without pituitary macroadenomas were seen primarily for evaluation of recent onset of impotence). In the macroadenoma group bromocriptine restored serum prolactin levels in 13 of the 16 and serum testosterone and potency in 5, whereas in the nontumor group it restored serum prolactin levels in all 10 and serum testosterone and potency in 9. (Author abstract) (19 Refs)

8. RECENT ADVANCES IN HORMONAL DETECTION OF PITUITARY SOMATOTROPIC ADENOMAS.

Turpin G, Heshmati H, De Gennes J
Service d'Endocrinologie-Metabolisme, Groupe Hospitalier Pite-Salpetriere, 47-83, boulevard de l'Hopital, F 75651 Paris, France
Ann Med Interne (Paris); 133(1):17-22 1982

Diagnostic hormonal tests were performed in 15 patients with acromegaly (8 men, 24-59 yr old, and 7 women, 27-62 yr old). The test group included 14 patients with macroadenomas of which 12 had been treated surgically and 2 were treated only with radiotherapy. One patient with a microadenoma was not treated. Following iv injection of thyrotropin releasing hormone (TRH), growth hormone (GH) increased in 9/15 cases between 50-2,650%. Prolactin increased in 13 cases between 50 and 900%. Following stimulation with luteinizing hormone releasing hormone, GH increased (54%) in one case, and prolactin did not increase in any cases. Following stimulation with Bromocriptine (BR), GH was blocked in seven cases between 52 and 97%. Prolactin was blocked in 11 cases. In five patients who had a positive response to TRH stimulation with BR followed by TRH led to secondary increase in prolactin secretion in response to TRH. The most reliable diagnostic tests are assays of basal GH and somatomedin levels, and the absence of blocking of GH by glucose. The tests described above could be valuable in the rare cases when the results of biological tests are inconclusive. (40 Refs) (In FRE)

9. BROMOCRIPTINE TREATMENT OF WOMEN WITH SUSPECTED PITUITARY PROLACTIN-SECRETING MICROADENOMAS.

Archer DF, Lattanzi DR, Moore EE, Harger JH, Herbert DL
Dept. Obstetrics adn Gynecology, Magee-Womens Hosp., Pittsburgh, PA, 15213
Am J Obstet Gynecol; 143(6):620-625 1982

The present study was designed to investigate the efficacy of bromocriptine in reducing serum prolactin (PRL) levels and in decreasing the size of PRL-secreting microadenomas. Bromocriptine, 5.0 mg, was administered daily for 2 years to 17 women who had galactorrhea, hyperprolactinemia, and hypocycloidal polytomographic evidence suggestive of a pituitary microadenoma. Serum PRL levels were normalized in 16 of 17 women during therapy. Associated with this was resumption of regular menses in 15 of 16 women with menstrual dysfunction and cessation of galactorrhea in 16 of the 17 women. Improvement in the roentgenographic appearance of the sella turcica occurred in two women. No progression in tumor size was found during the course of therapy. Side effects attributed to bromocriptine were minimal, transient, and usually well tolerated. These data suggest that bromocriptine is an appropriate therapeutic modality for PRL-secreting pituitary microadenomas. (Author abstract) (16 Refs)

OTHER THERAPY OF CNS MALIGNANCIES

10. A SURGICAL APPROACH TO CHORDOMAS AT THE BASE OF THE SKULL.

Miller RH, Woodson GE, Neely G, Murphy EC
Dept. Otorhinolaryngology and Communicative Sciences, Baylor Coll. Medicine, Texas Medical Center, Houston, TX, 77030
Otolaryngol Head Neck Surg; 90(2):251-255 1982

Massive recurrent chordoma involving the intracranial cavity, nasal cavity, and maxillary antrum was diagnosed in a 69-yr-old woman with left-sided facial swelling and nasal obstruction. The patient had a 2-yr history of left-sided parietal headaches and hoarseness, and the patient's family noted a marked deterioration of the patient's mental status. A diagnosis of chondroid chordoma was made. The intracranial portion of the tumor was carefully debulked through the floor of the middle cranial fossa. The patient has been followed-up for 2 yr with no recurrence of the symptoms and with normal remodeling of the face and palate. (16 Refs)

OTHER CLINICAL ASPECTS OF CNS CANCER

11. CLINICAL NMR IMAGING OF THE BRAIN: 140 CASES.

Bydder GM, Steiner RE, Young IR, Hall AS, Thomas DJ, Marshall J, Pallis CA, Legg NJ
(c/o Steiner) Dept. Diagnostic Radiology, Royal Postgraduate Medical Sch., Du Cane Road, London W12 OHS, England

AJR; 139(2):215-236 1982

Cranial nuclear magnetic resonance (NMR) scans were performed on 13 healthy volunteers and 140 patients with a broad spectrum of neurologic disease and compared with x-ray computed tomography (CT) scans. The NMR scans included a variety of sequences reflecting proton density, blood flow, T1, and T2 as well as transverse, sagittal, and coronal images. White matter, gray matter, and cerebrospinal fluid were clearly distinguished in the normal brain with inversion-recovery (IR) sequences, and normal progressive myelination was demonstrated in infants and children. Acute hemorrhages displayed short T1 values, but other pathologic processes were associated with long T1 values. Cysts had very long T1 values. Spin-echo (SE) sequences showed increased values of T2 in a variety of conditions and highlighted lesions against the relatively featureless background of the remaining brain. With inversion-recovery scans, different stages of infarction were recognized in the hemispheres. NMR was more useful than CT in demonstrating brainstem infarction. The white matter lesions in demyelinating diseases were well demonstrated with NMR scans. Benign tumors were well seen and usually had shorter T1 values than malignant tumors. Mass effects from tumors were generally better demonstrated with NMR than with CT, including more subtle mass effects such as displacement of the external capsule. Abnormalities were seen in diseases of the basal ganglia, including marked atrophy of the head of the caudate nucleus in Huntington chorea. Advantages of NMR imaging include the high level of gray-white matter contrast, lack of bone artifact, variety of possible sequences, transverse, sagittal, and coronal imaging, sensitivity to pathologic change, and lack of known hazard. Disadvantages include lack of bone detail, limited spatial resolution, lack of contrast agents, and cost. NMR seems to be a potentially important addition to existing techniques of neurologic diagnosis. (44 Refs)

12. COMPUTED TOMOGRAPHY OF 'CYSTIC' INTRAMEDULLARY LESIONS.

Pullicino P, Kendall BE
Lysholm Radiological Dept., Natl. Hosp. Nervous Diseases, Queen Square, London WC 1, England

Neuroradiology; 23(3):117-121 1982

Using an EMI 5005 scanner with higher resolution option, 75% of syrinxes were shown as low density cavities. Most spinal cord tumors caused isodense swellings, but 41% contained low density zones and cystic elements were demonstrated in 76% of these at surgery or by puncture of the spinal cord; a few (11%) of the isodense tumors were cystic. The differential diagnosis of low density intramedullary lesions is discussed. (Author abstract) (15 Refs)

13. COMPUTED TOMOGRAPHY OF INTRACRANIAL LYMPHOMA.

Thomas M, Macpherson P
Dept. Neurology, Inst. Neurological Sciences, Southern General Hosp., Glasgow, Scotland

Clin Radiol; 33(3):331-336 1982

The appearances on computed tomography (CT) of 17 patients with histologically proven intracranial lymphoma have been analyzed and abnormalities detected in 16. Four of the patients had systemic lymphoma. Multiple lesions were seen in eight patients (47%), in six of whom the multiple lesions in each patient were of similar appearance. There was good macroscopic correlation between the CT and post-mortem appearances in the eight patients who subsequently died, although in five, histological examination showed more extensive infiltration. Meningeal involvement was seen more commonly in the cases of systemic lymphoma than in the purely cerebral lymphomas, but parenchymal lesions were equally common in both. Grey matter lesions tended to be clearly demarcated, of increased density with little edema or displacement; homogeneous density enhancement was produced by the intravenous injection of contrast medium. White matter lesions were usually poorly demarcated, of variable density with marked edema and displacement, and with heterogeneous enhancement. (Author abstract) (18 Refs)

14. INTRAOPERATIVE SONOGRAPHY FOR BRAIN TUMOR LOCALIZATION AND VENTRICULAR SHUNT PLACEMENT.

Knake JE, Chandler WF, McGillicuddy JE, Silver TM, Gabrielsen TO
Dept. Radiology, Univ. Michigan Hospitals, Ann Arbor, MI, 48109

AJNR; 3(4):425-430 1982

Efficacy of intraoperative sonography was evaluated in 16 patients with various cerebral lesions. Of 16 patients, 1 had ganglioglioma, 5 had Grade I-II astrocytoma, 1 had endodermal sinus tumor, 1 had arteriovenous malformation, 6 had brain metastases from lung, breast, and kidney carcinoma, 1 had undifferentiated small cell metastases, and 1 had unclassifiable malignant glial tumor. Tumor size ranged from less than 2.5 cm in 10 patients to 2.5-4.0 cm in 5, and 4 x 6 cm in 1. The transducer was first applied to the intact dura or to the exposed brain surface. The sonography was repeated after opening the dura. All solid cerebral masses were mildly hyperechoic in relation to the surrounding brain tissue. Three tumors had detectable calcification, and half of the tumors caused reactive brain edema. Intraoperative sonography did not provide any additional information on the differential diagnosis of brain lesions. The advantage of intraoperative sonography was associated with precise localization of small lesions and with the ability to monitor the placement of the ventricular catheter. (6 Refs)

15. INVESTIGATION OF AN APPARENT INCREASED PREVALENCE OF BRAIN TUMORS IN A U. S. PETROCHEMICAL PLANT.

Alexander V, Leffingwell SS, Lloyd JW, Waxweiler RJ, Miller RL
Occupational Safety and Health Admin., United States Dept. Labor, Washington, DC, 20210

Ann NY Acad Sci; 381:97-107 1982

The occurrence of 20 primary brain cancer deaths among workers in a moderate-sized petrochemical production facility in Texas prompted a cohort mortality study and a brain tumor case-control study. The av age at death was 55 yr and the total length of employment ranged from 1 mo to greater than 35 yr, with a median value of 19 yr. The interval from first employment to death ranged from 3.5 yr to almost 36 yr, with a median of 24 yr. All cases were males; 18 were white, 2 black. All but one were native-born Americans. Comparison with county primary brain tumor death statistics revealed an approx plant-wide risk about 2x that of the county as a whole. Sixteen of the cases were identified as glioblastoma multiforme. No common job title, department code, or chemical exposure could be found in careful preliminary examination of the work histories of the affected employees. Potential suspect agents which could be responsible for the unusual occurrence of brain cancer at this plant include vinyl chloride and diethyl sulfate; however, careful examination of the work histories did not support a significant positive association with vinyl chloride. These tumors are likely the result of occupational chemical exposures since there is no good evidence implicating nonplant, general environmental factors as the cause of brain cancer excess. (57 Refs)

16. BRAIN CANCER AMONG OCAW MEMBERS IN THREE TEXAS OIL REFINERIES.

Thomas TL, Waxweiler RJ, Crandall MS, White DW, Moure-Eraso R, Itaya S, Fraumeni JF
Environmental Epidemiology Branch, NCI, Bethesda, MD, 20205
Ann NY Acad Sci; 381:120-129 1982

The risk of brain cancer was investigated in populations of active and retired members of the Oil, Chemical, and Atomic Workers International Union (OCAW) employed in three Texas oil refineries and a case-control study of brain cancer deaths among active union members at two of the refineries. The proportionate mortality ratio (PMR: the ratio of observed to expected deaths), the proportionate cancer mortality ratio (PCMR), and the local two-county PCMR (CPCMR) were determined. PMR's for total cancer and circulatory diseases were significantly elevated and more prominent among active than retired union members. There were 27 deaths from malignant brain cancer compared with expected deaths of 11.8, 14.7, 18.4 in the PMR, PCMR and CPCMR groups, respectively. The difference between observed and expected brain tumor deaths was significant only for active members. Both PMR and PCMR were significantly elevated among active members in the three refineries combined. At two refineries, there was greater than two-fold relative excess in brain tumor deaths among union members. Brain tumor deaths were excessive among all age groups, but the PMR was significant only among decedents in the 50-64-yr age group. The case-control study of two refineries suggested three employment categories at increased risk for brain tumors: the 'motor oil' category, the 'maintenance and labor' category, and the 'receipt and movement' category. However, the numbers of individuals in this study were small. More definitive studies are necessary to determine the risks and identify the specific exposures that may be responsible. (17 Refs)

SELECTED PRECLINICAL ASPECTS OF CNS CANCER

17. TOLERANCE OF THE CENTRAL NERVOUS SYSTEM TO PHOTON IRRADIATION. ENDOCRINE COMPLICATIONS.

Wigg DR, Murray RM, Koschel K
Radiotherapy Dept., Royal Adelaide Hosp., North Terrace, Adelaide 5000, Australia
Acta Radiol Oncol Radiat Phys Biol; 21(1):49-60 1982

Dose-response isoeffect equations have been determined for hypothalamic pituitary insufficiency following cranial irradiation. Of particular importance is the occurrence of complications at doses substantially less than those commonly used for the treatment of central nervous system tumors. Such complications may be severe and potentially life threatening. These complications occur when a small midline 'target' vol containing the pituitary gland, infundibulum and adjacent inferior hypothalamic structures is irradiated. Direct pituitary irradiation is unlikely to be a factor, at least in some cases. The possible role of incidental hypothalamic irradiation in the control of acromegaly and pituitary dependent Cushing's syndrome is discussed. (Author abstract) (53 Refs)

18. SENSITIVITY TO 1-(4-AMINO-2-METHYL-5-PYRIMIDINYL)METHYL-3-(2 CHLOROETHYL)-3-NITROSOUREA HYDROCHLORIDE (ACNU) OF GLIOMA CELLS IN VIVO AND IN VITRO.

Yoshida J, Shibuya N, Kobayashi T, Kageyama N
Dept. Neurosurgery, Nagoya Univ. Sch. Medicine, 65, Tsurumai-cho, Show-Ku, Nagoya, Japan
Cancer; 50(3):410-418 1982

A new water-soluble nitrosourea (1-(4-amino-2-methyl-5-pyrimidinyl)methyl-3-(2 chloroethyl)-3-nitrosourea hydrochloride, ACNU) was tested for its antitumor activity against four glioma cell lines. Four factors were studied to determine its antitumor activity: inhibition of cell growth, morphologic observation, analysis of DNA histogram with flow microfluorometry, and sensitivity testing with microtest plate. Growth inhibition in response to ACNU was seen in two cell lines (EA-285, U251-MG), whereas two cell lines (YE2-2, T98) were resistant to ACNU. The results of the present sensitivity test concur with those of other examinations that this test is useful in selecting a drug and determining the effective dose. (Author abstract) (21 Refs)

19. CURRENT APPROACHES TO THE EXPERIMENTAL INVESTIGATION OF CHEMICALS IN RELATION TO CANCER OF THE BRAIN.

Swenberg JA, Zimmerman HM, Maltoni C, Kurland L, Laerum OD, Kleihues P, Selikoff I, Heidelberger C
Chemical Industry Inst. Toxicology, Research Triangle Park, NC, 27709
Ann NY Acad Sci; 381:43-53 1982

Chemical induction of brain tumors, current methods for evaluating the carcinogenic potential of chemicals, and possible mechanisms of neuro-oncogenesis are reviewed. Chemical induction of brain tumors by polycyclic aromatic hydrocarbons, nitroso compounds, acrylonitrile, and other chemicals (1-aryl-3,3-dialkyltriazenes, 1,2-diethylhydrazine, azoethane, azoxyethane, and procarbazine) is described. Only a small number of chemicals that induce brain tumors have been identified by routine bioassays of new chemicals. Current guidelines require

exposure of a minimum of 50 animals of each sex to 2-3 exposure levels and an equal number of controls. Complete necropsies, diagnosis by an experienced histopathologist, and confirmatory histochemical techniques are essential for properly classified brain tumors. Knowledge of normal variation in tumor incidence between species, strain, and sex is required. A positive bioassay should induce a significantly increased incidence of tumors in a dose-related manner. Possible mechanisms involved in neuro-oncogenesis have been proposed, including the formation and persistance of O6-alkylguanine in brain DNA of rodents and the occurrence of glial cell replication in the presence of promutagenic DNA damage. (48 Refs)

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